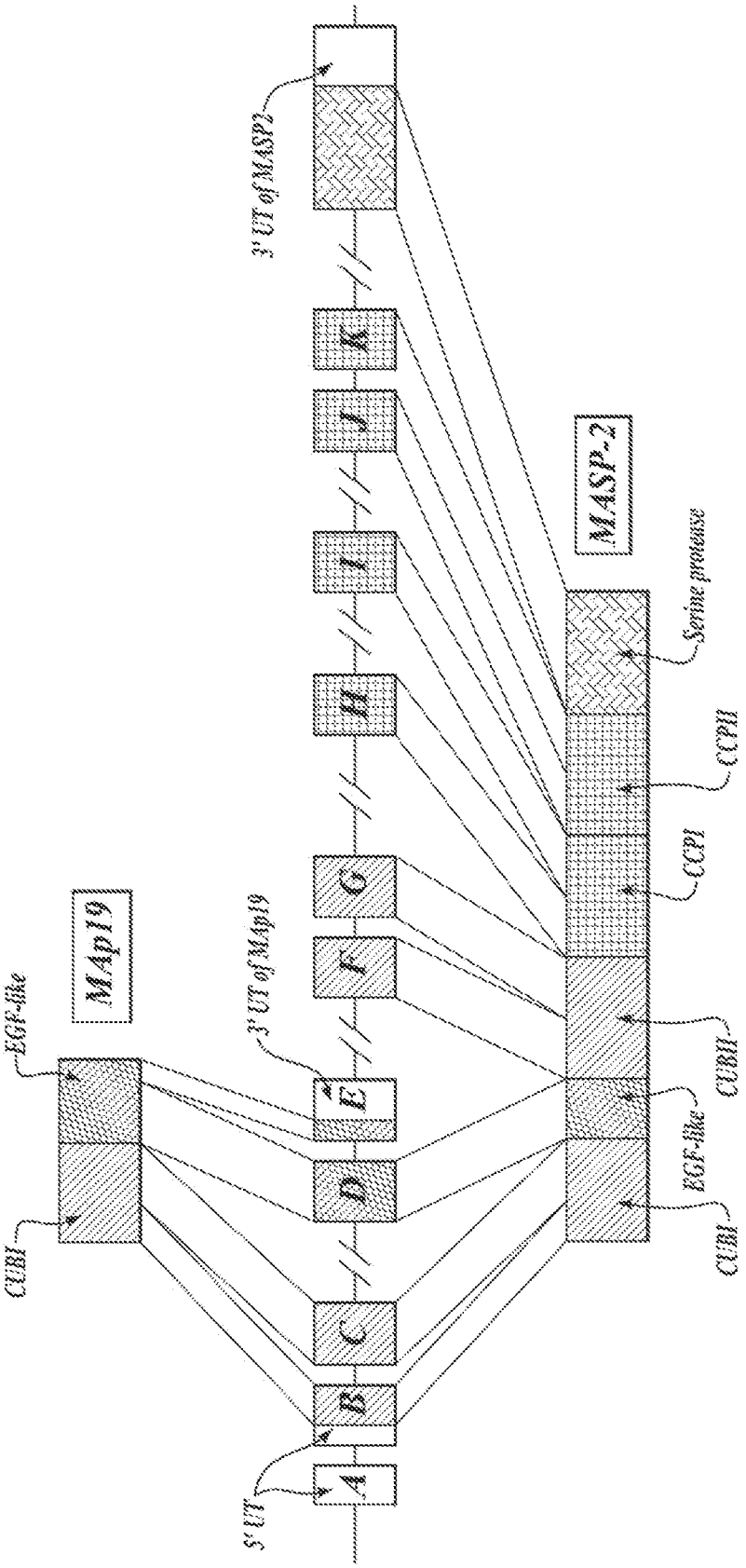

MAp19
EGF-like
CUBI
5' UT
A
B
C
D
E
F
G
H
I
J
K
3' UT of MAp19
3' UT of MASP2
MASP-2
Serine protease
CCPII
CCPI
CUBII
EGF-like
CUBI

FIG. 1

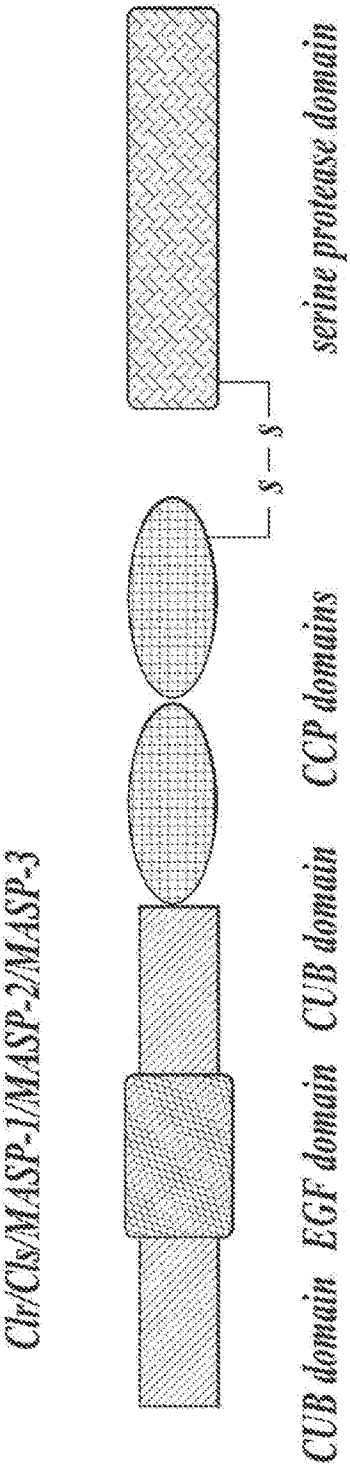

Clr/Cls/MASP-1/MASP-2/MASP-3
CUB domain
EGF domain
CUB domain
CCP domains
S — S
serine protease domain

FIG. 2A

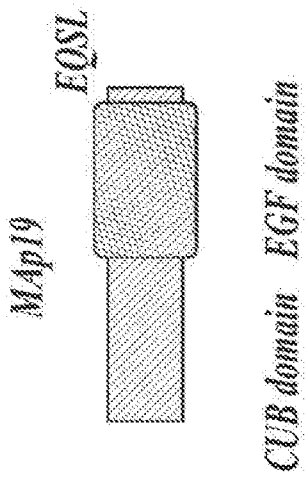

MAp19
EQSL
CUB domain
EGF domain

FIG. 2B

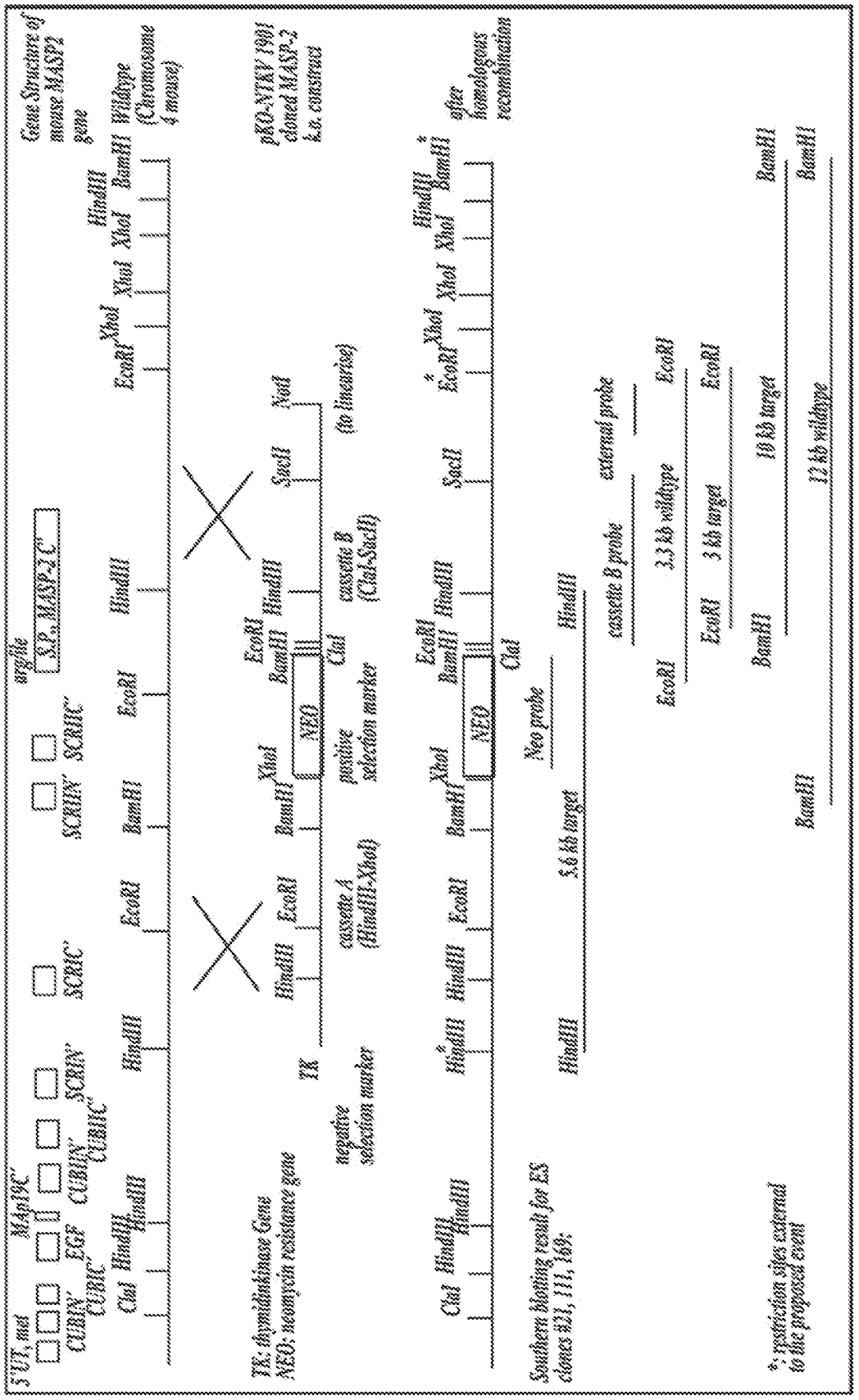

Gene Structure of mouse MASP2 gene
Wildtype (Chromosome 4 mouse)
pKO-NTKV 1901 cloned MASP-2 k.o. construct
after homologous recombination
Southern blotting result for ES clones #31, 111, 169:
5.6 kb target
Neo probe
cassette B probe
external probe
3.3 kb wildtype
3 kb target
10 kb target
12 kb wildtype
TK; thymidinkinase Gene
NEO; neomycin resistance gene
negative selection marker
positive selection marker
cassette A (HindIII-XhoI)
cassette B (ClaI-SacII)
(to linearize)
*; restriction sites external to the proposed event

FIG. 3

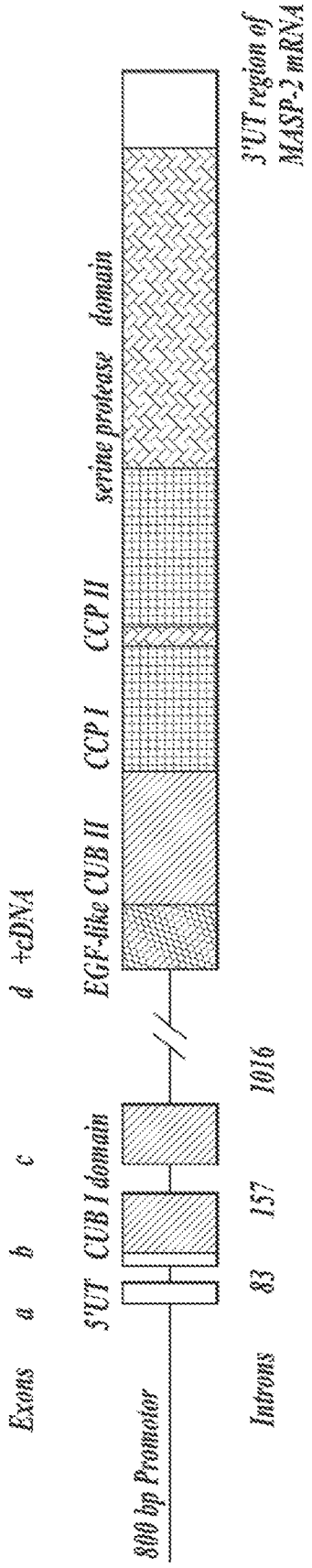

Exons a b c d +cDNA
5'UT CUB I domain EGF-like CUB II CCP I CCP II serine protease domain
3'UT region of MASP-2 mRNA
800 bp Promoter
Introns 83 157 1016

FIG. 4

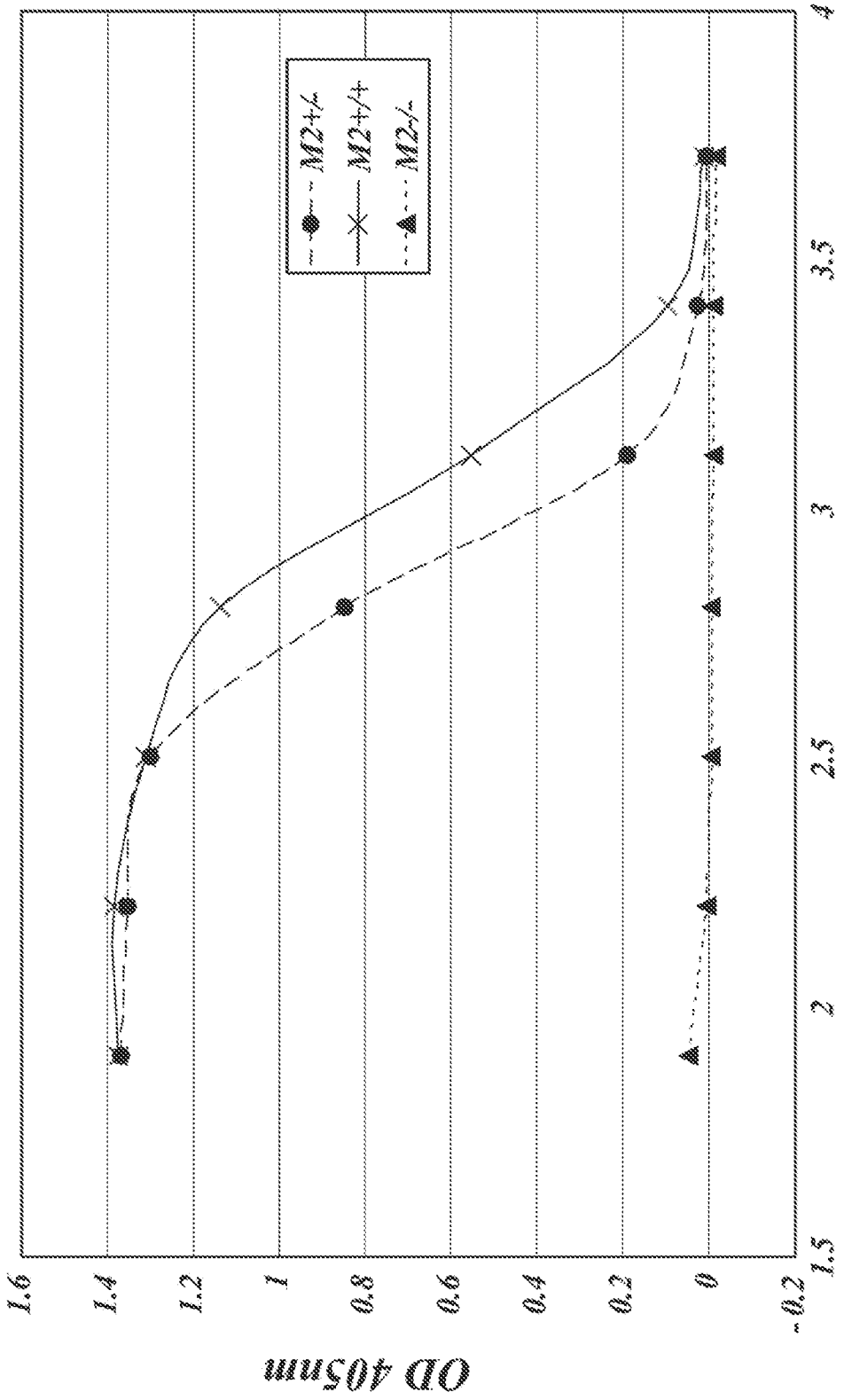

M2+/+
M2+/-
M2-/-
OD 405nm
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
-0.2
log serum dilutions
1.5
2
2.5
3
3.5
4

FIG. 5A

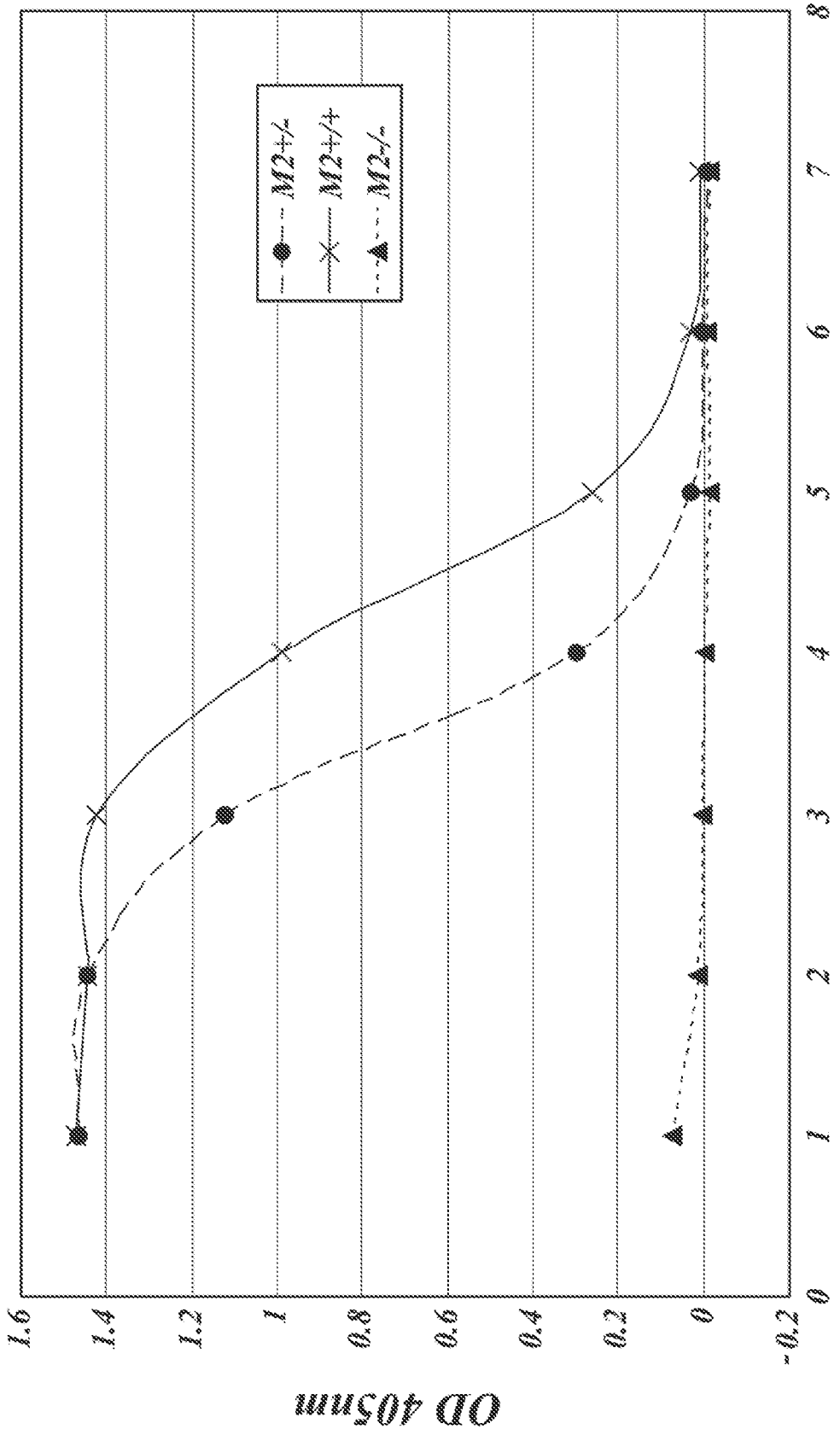

M2+/+
M2+/-
M2-/-
OD 405nm
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
-0.2
0
1
2
3
4
5
6
7
8
log serum dilutions

FIG. 5B

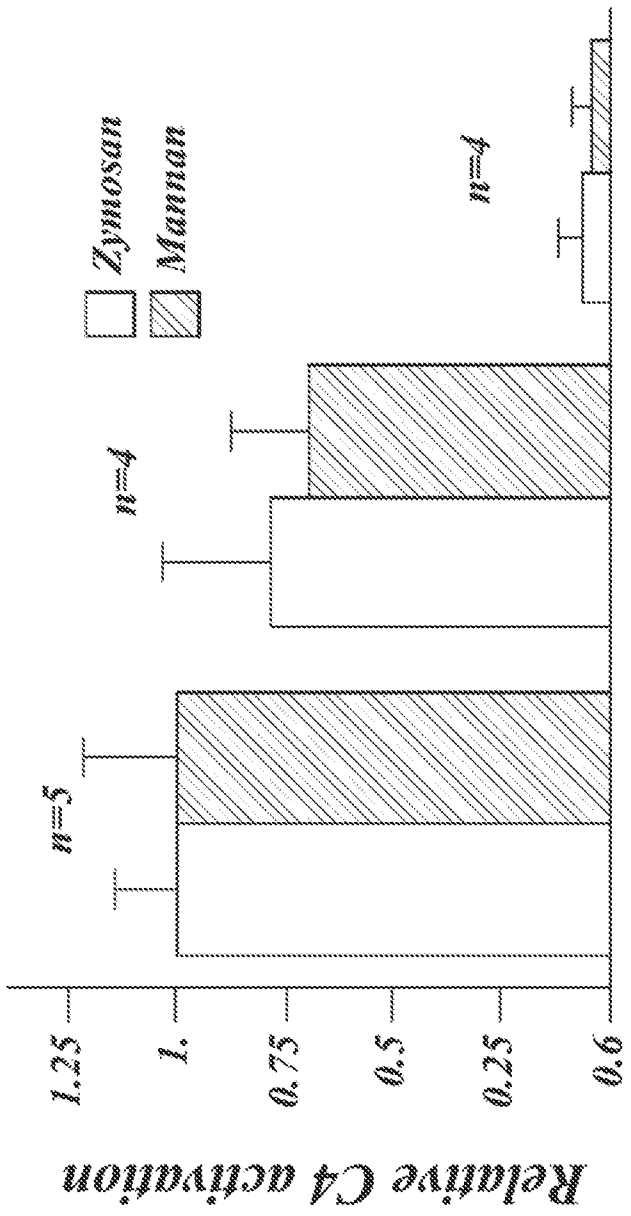

Relative C4 activation
1.25
1.
0.75
0.5
0.25
0.6
n=5
n=4
n=4
Zymosan
Mannan
WT
M2 +/-
M2 -/-

FIG. 5C

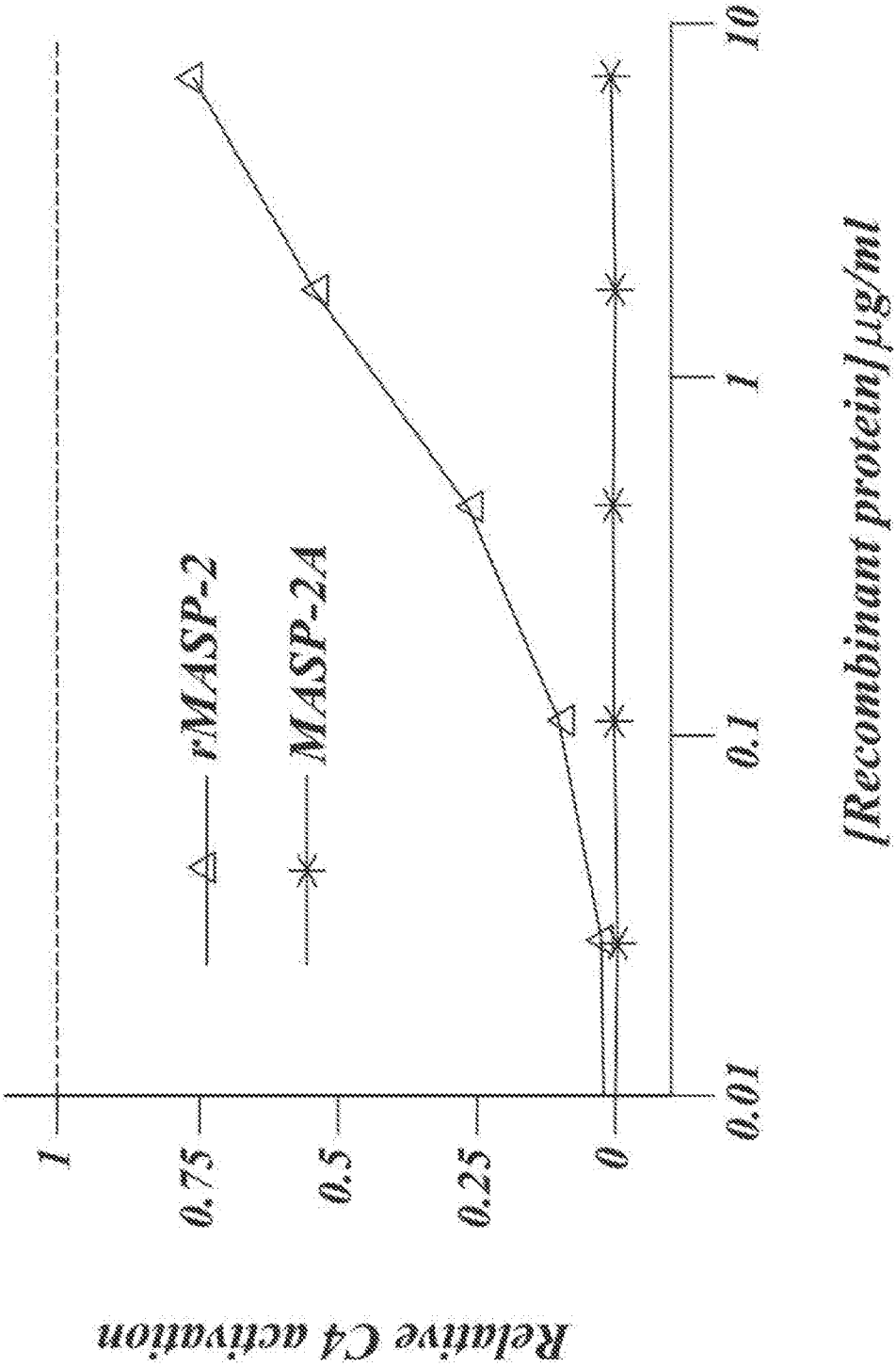

Relative C4 activation
1
0.75
0.5
0.25
0
0.01
0.1
1
10
[Recombinant protein] µg/ml
rMASP-2
MASP-2A

FIG. 6

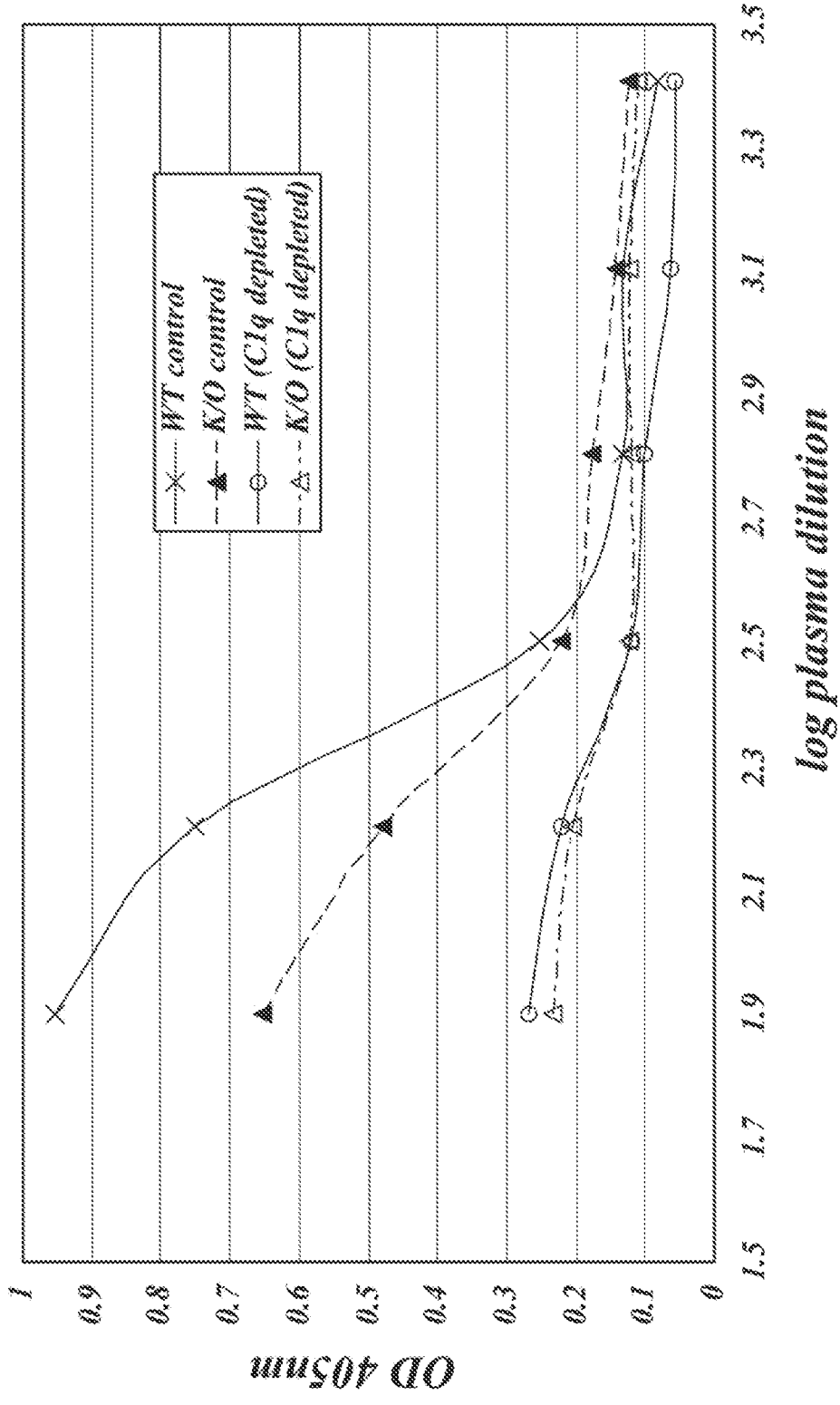

OD 405nm
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
1.5
1.7
1.9
2.1
2.3
2.5
2.7
2.9
3.1
3.3
3.5
log plasma dilution
WT control
K/O control
WT (C1q depleted)
K/O (C1q depleted)

FIG. 7

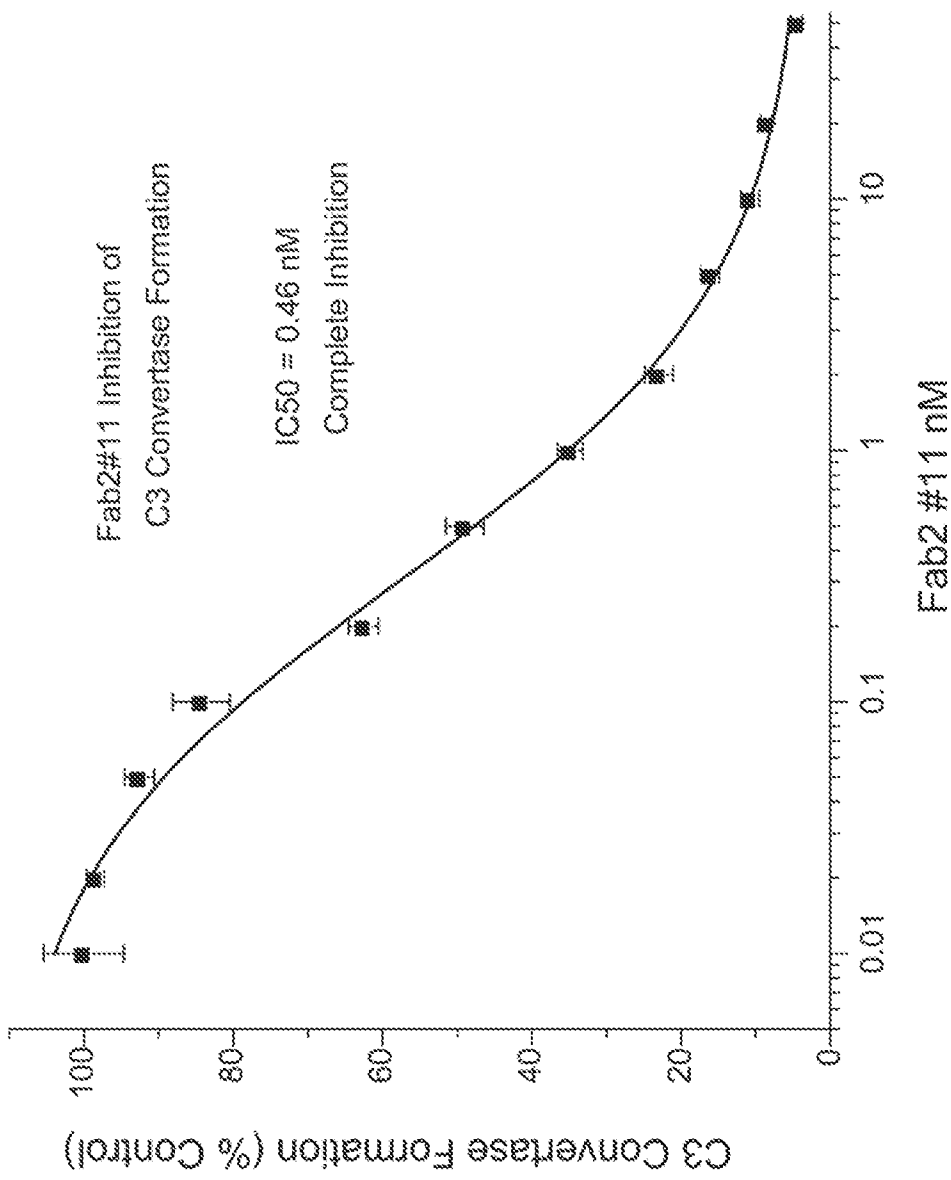

Fab2#11 Inhibition of
C3 Convertase Formation
IC50 = 0.46 nM
Complete Inhibition
C3 Convertase Formation (% Control)
100
80
60
40
20
0
0.01
0.1
1
10
Fab2 #11 nM

FIG. 8A

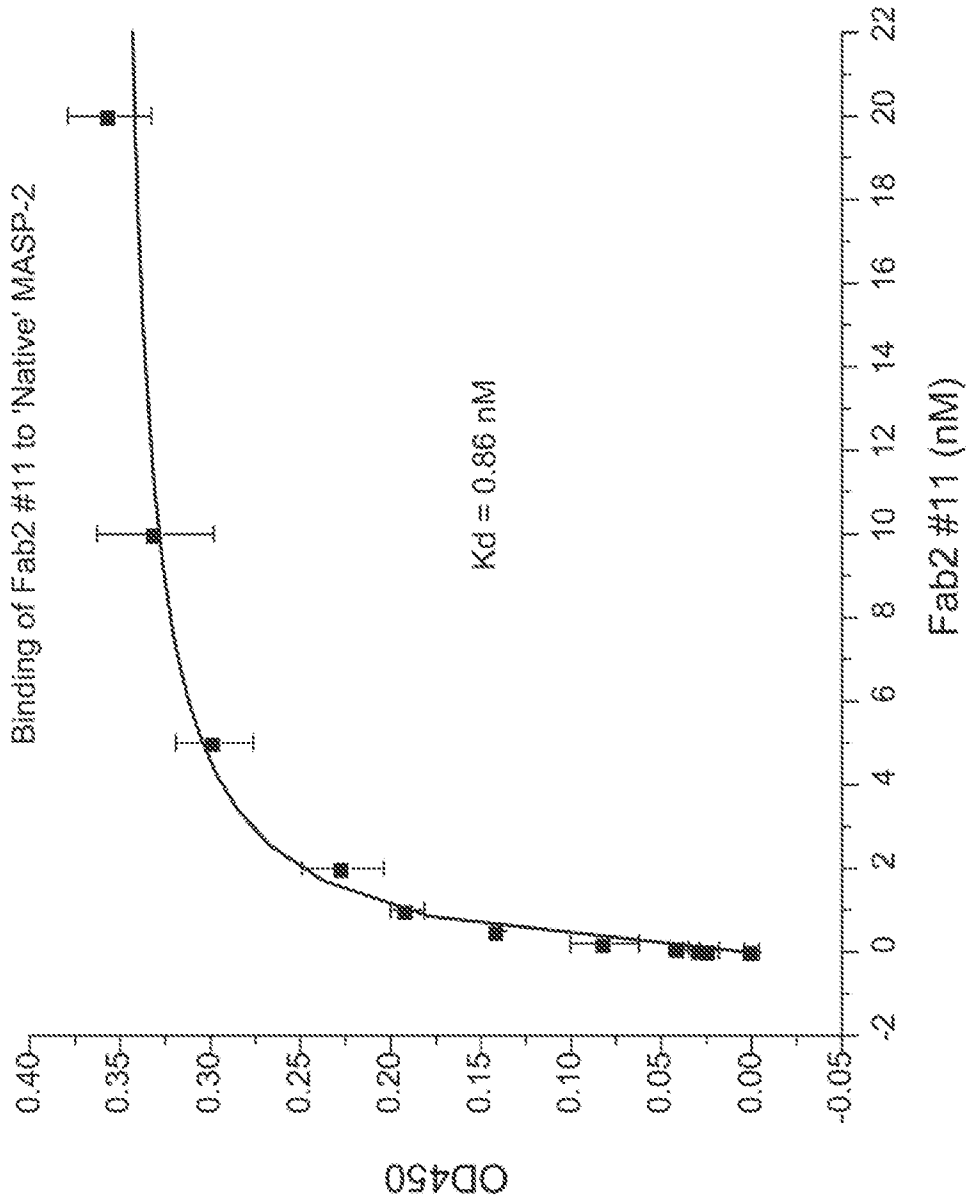

Binding of Fab2 #11 to 'Native' MASP-2
Kd = 0.86 nM
OD450
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
-0.05
-2
0
2
4
6
8
10
12
14
16
18
20
22
Fab2 #11 (nM)

FIG. 8B

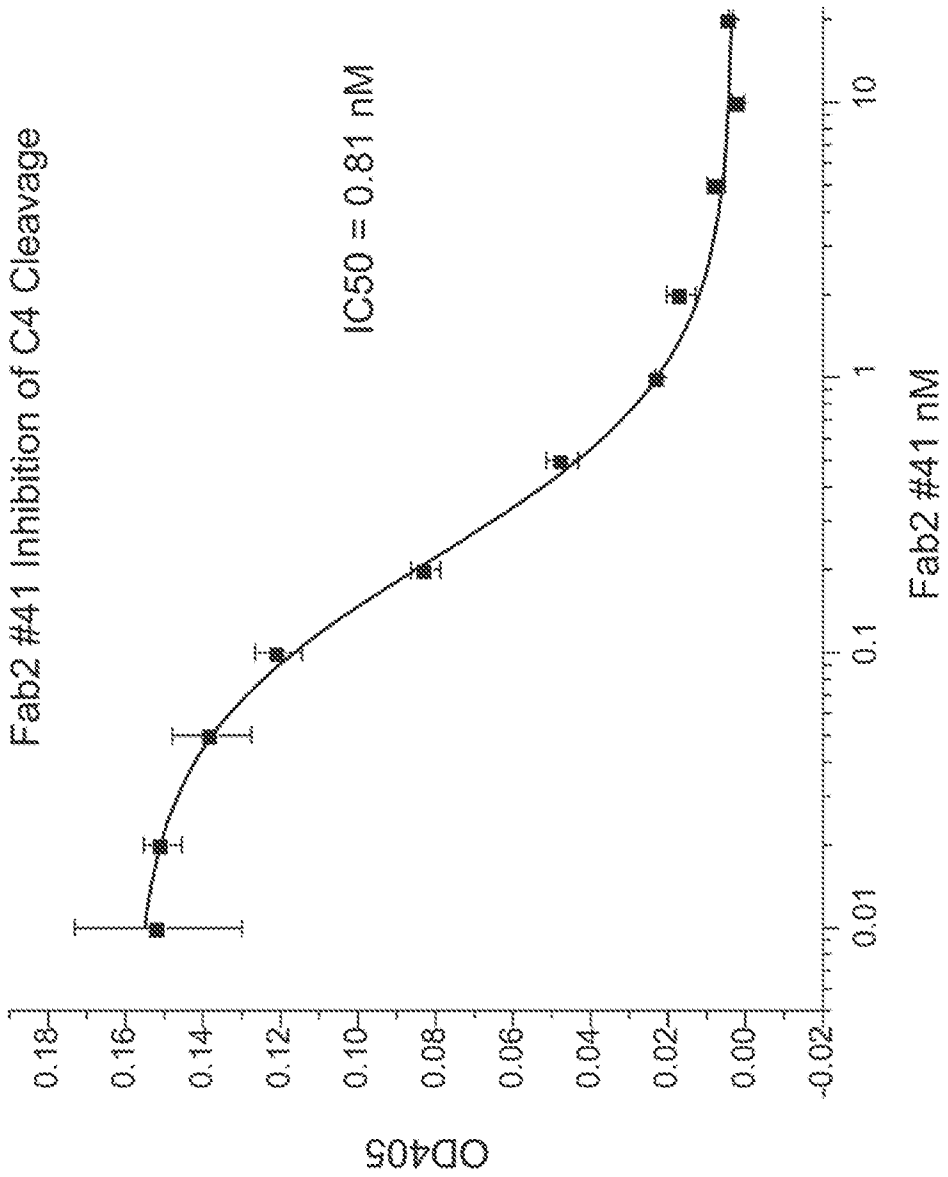

Fab2 #41 Inhibition of C4 Cleavage
IC50 = 0.81 nM
OD405
0.18
0.16
0.14
0.12
0.10
0.08
0.06
0.04
0.02
0.00
-0.02
0.01
0.1
1
10
Fab2 #41 nM

FIG. 8C

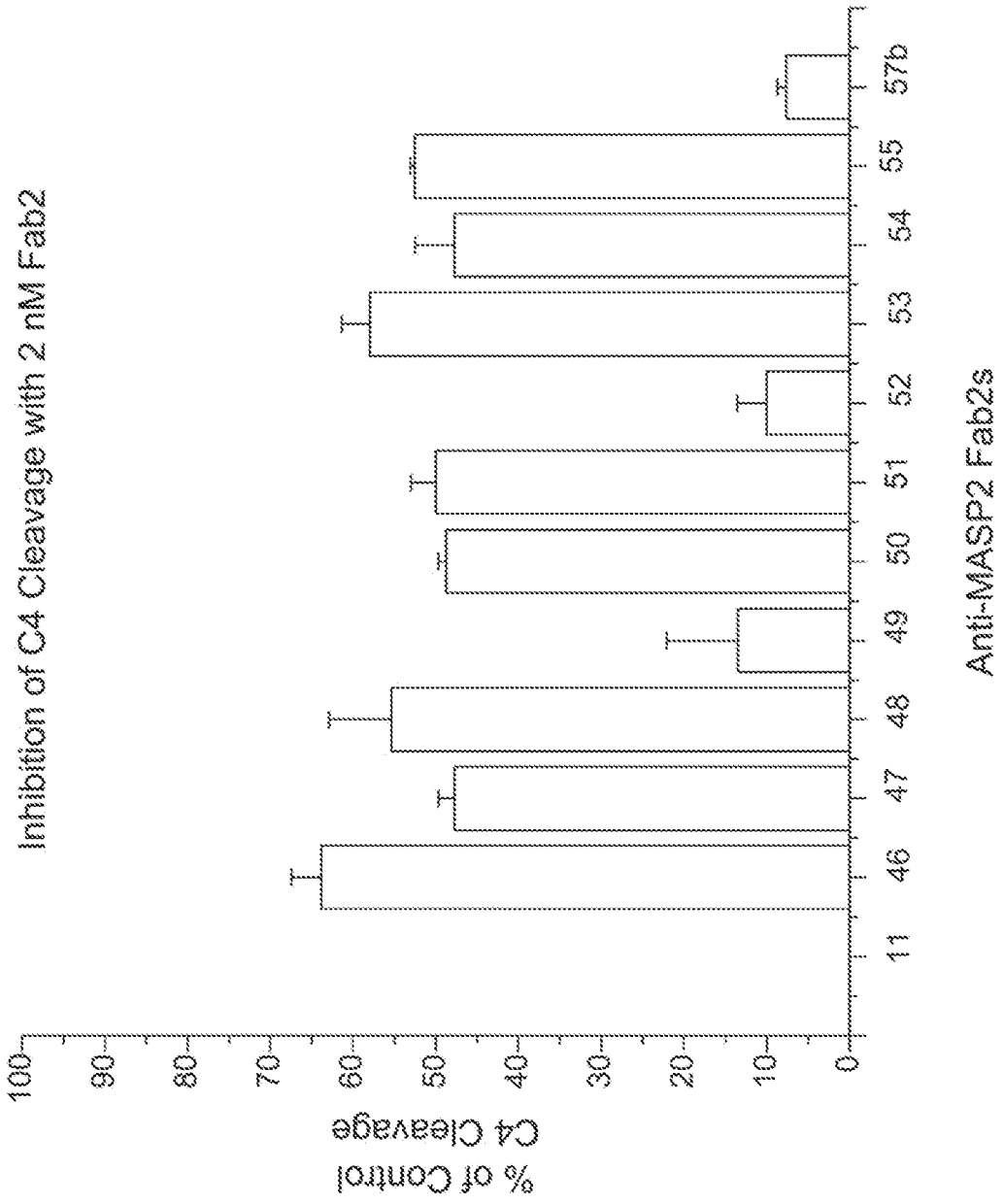

Inhibition of C4 Cleavage with 2 nM Fab2
% of Control C4 Cleavage
100
90
80
70
60
50
40
30
20
10
0
11
46
47
48
49
50
51
52
53
54
55
57b
Anti-MASP2 Fab2s

FIG. 9

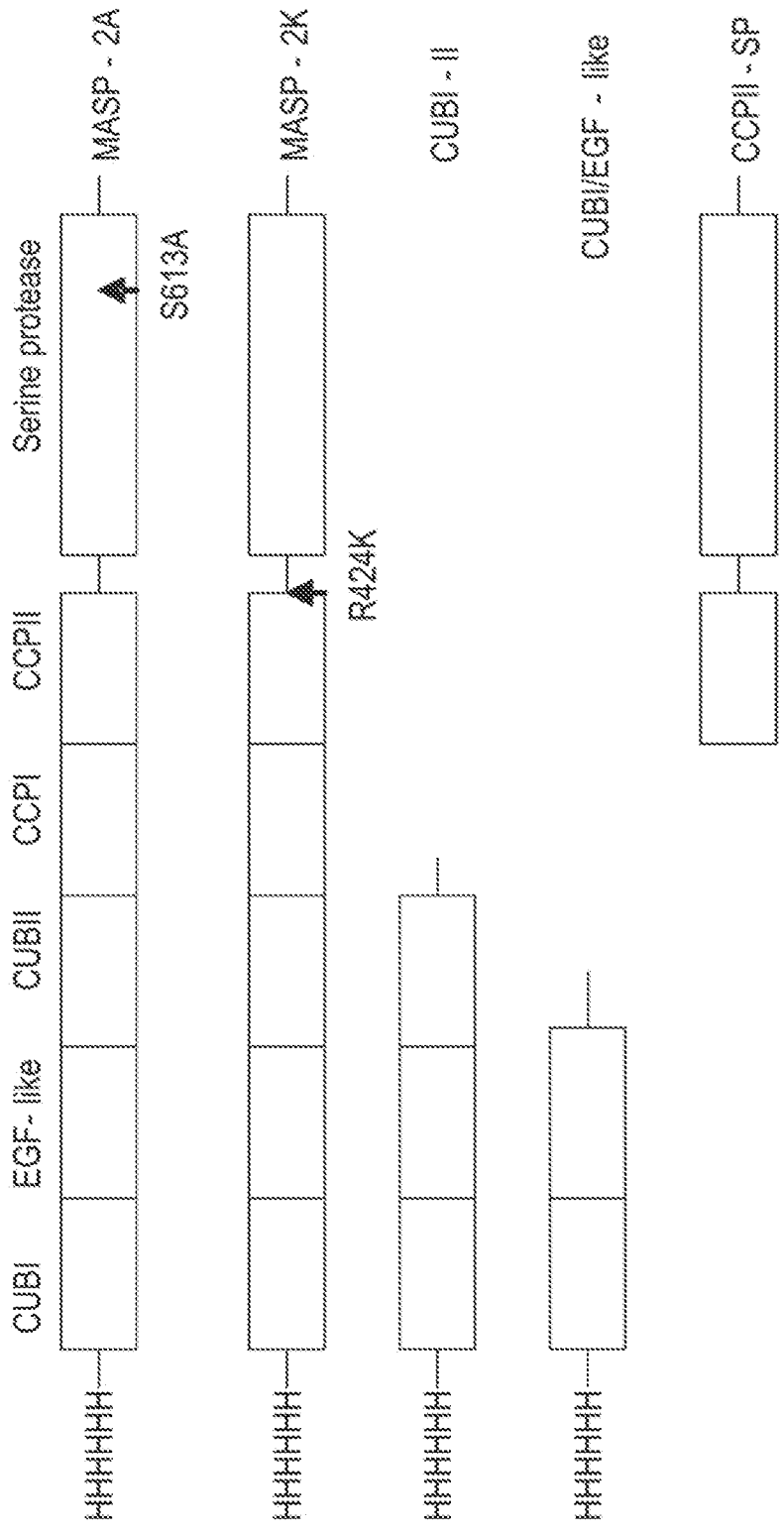

CUBI
EGF- like
CUBII
CCPI
CCPII
Serine protease
MASP - 2A
S613A
HHHHHH
MASP - 2K
R424K
HHHHHH
CUBI - II
HHHHHH
CUBI/EGF - like
HHHHHH
CCPII - SP

FIG. 10

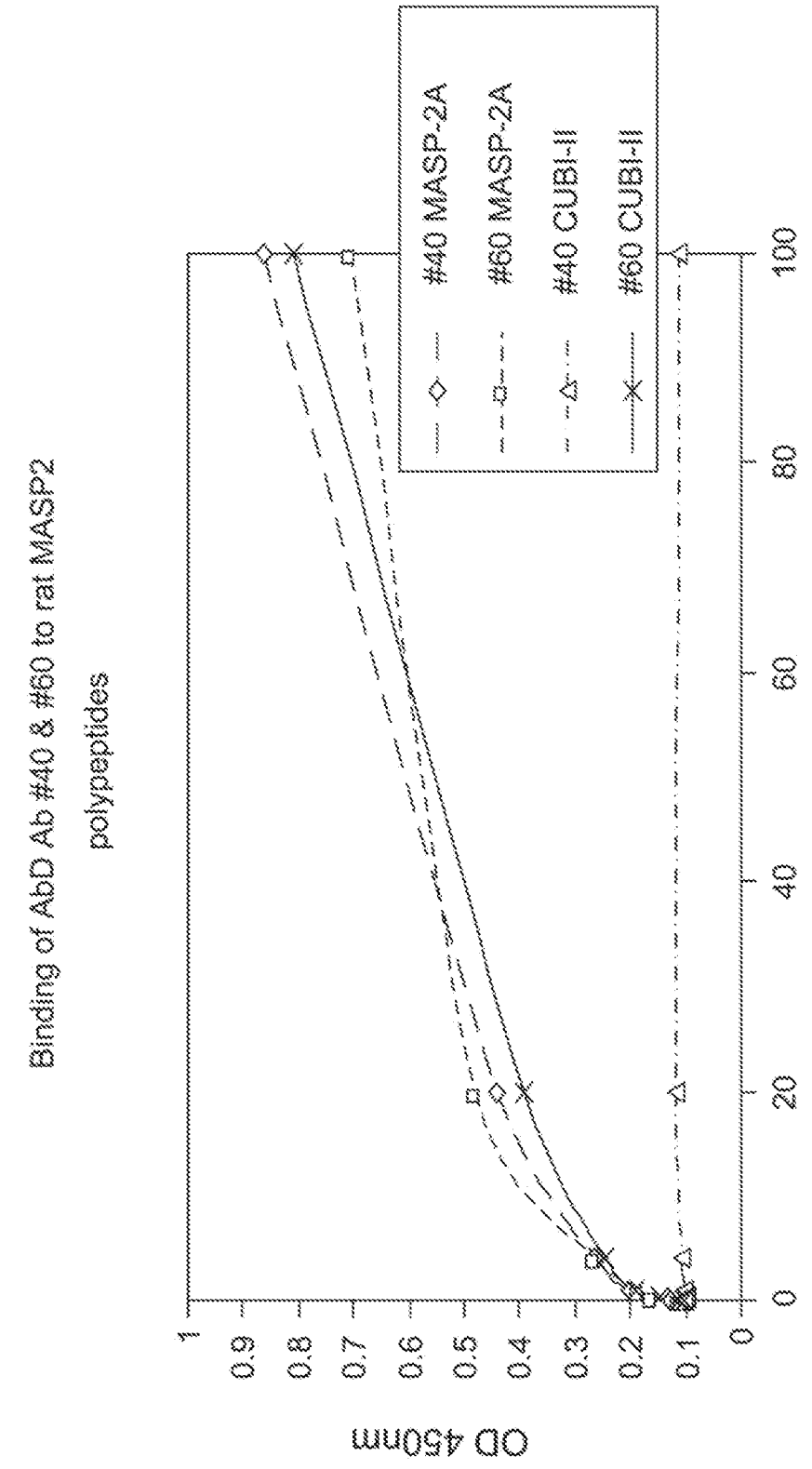

Binding of AbD Ab #40 & #60 to rat MASP2
polypeptides
#40 MASP-2A
#60 MASP-2A
#40 CUBI-II
#60 CUBI-II
OD 450nm
[Ab] nM
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
0
20
40
60
80
100

FIG. 11

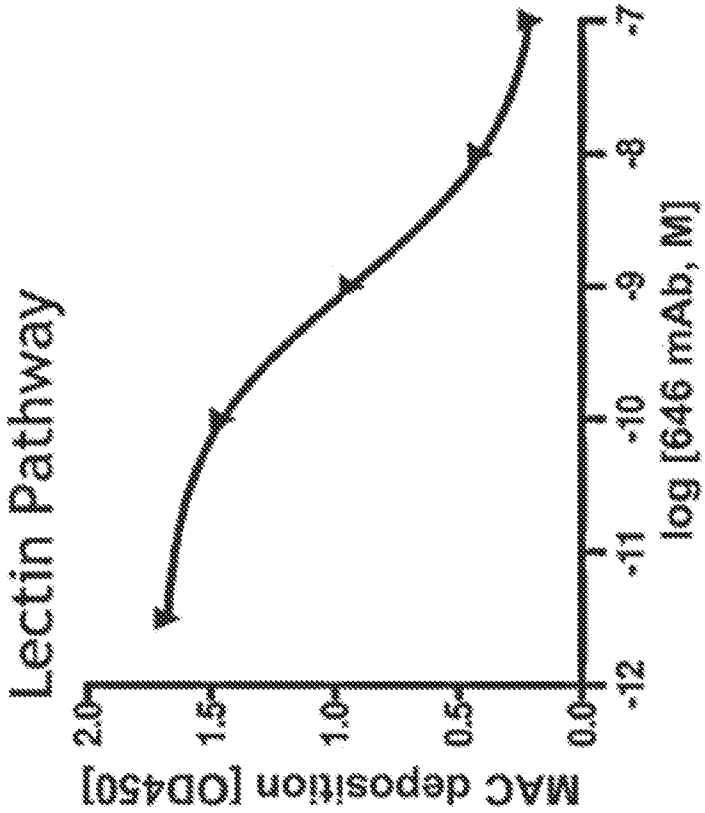

Lectin Pathway
MAC deposition [OD450]
2.0
1.5
1.0
0.5
0.0
-7
-8
-9
-10
-11
-12
log [646 mAb, M]

FIG. 12A

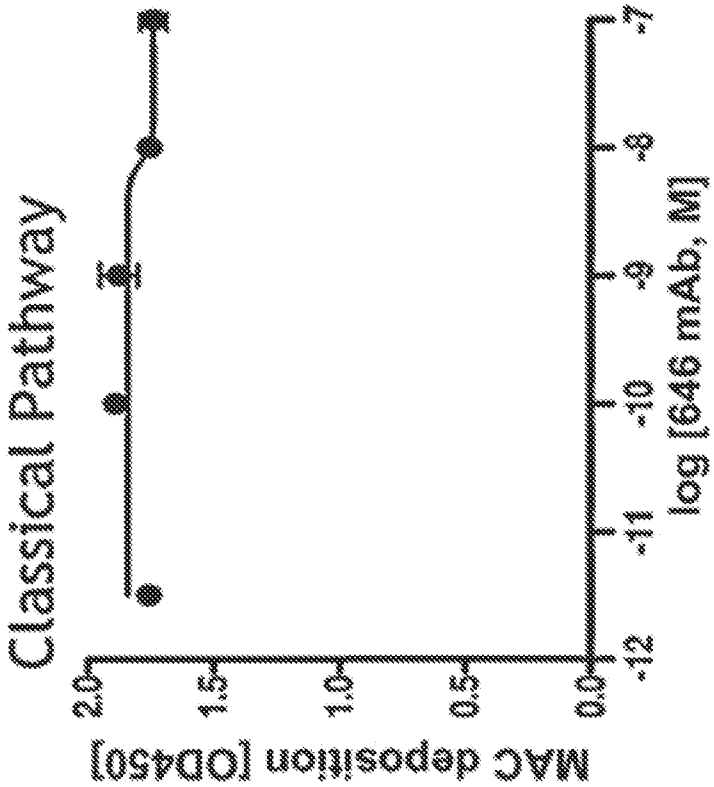

Classical Pathway
MAC deposition [OD450]
2.0
1.5
1.0
0.5
0.0
-12
-11
-10
-9
-8
-7
log [646 mAb, M]

FIG. 12B

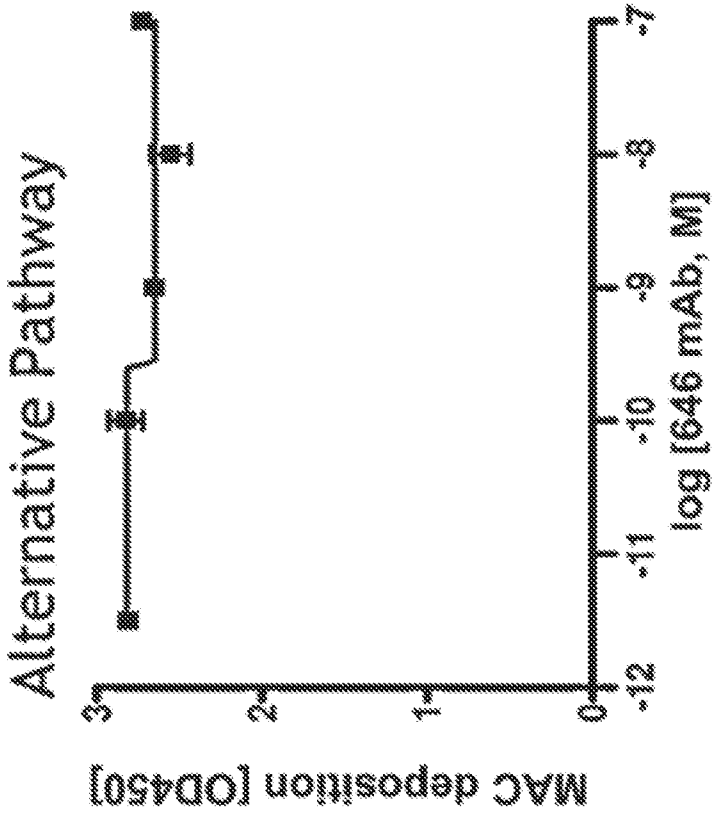

Alternative Pathway
MAC deposition [OD450]
3
2
1
0
-7
-8
-9
-10
-11
-12
log [646 mAb, M]

FIG. 12C

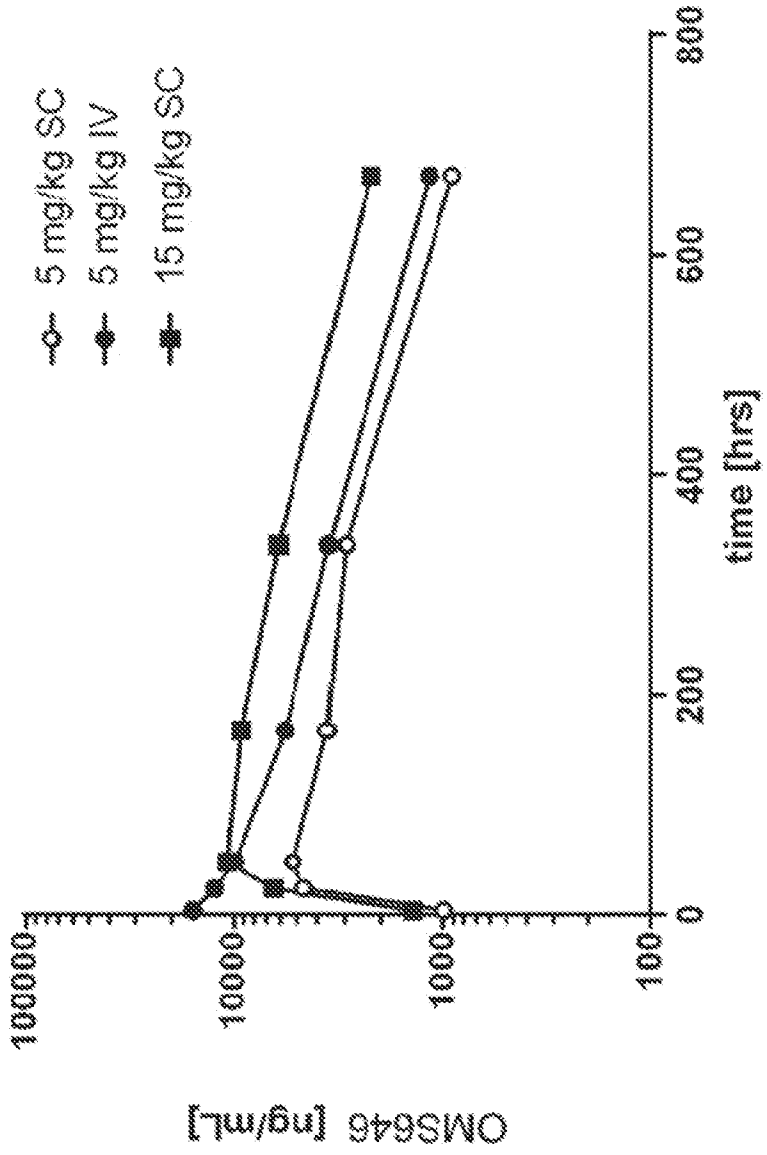

5 mg/kg SC
5 mg/kg IV
15 mg/kg SC
100000
10000
1000
100
0
200
400
600
800
time [hrs]
OMS646 [ng/mL]

FIG. 13

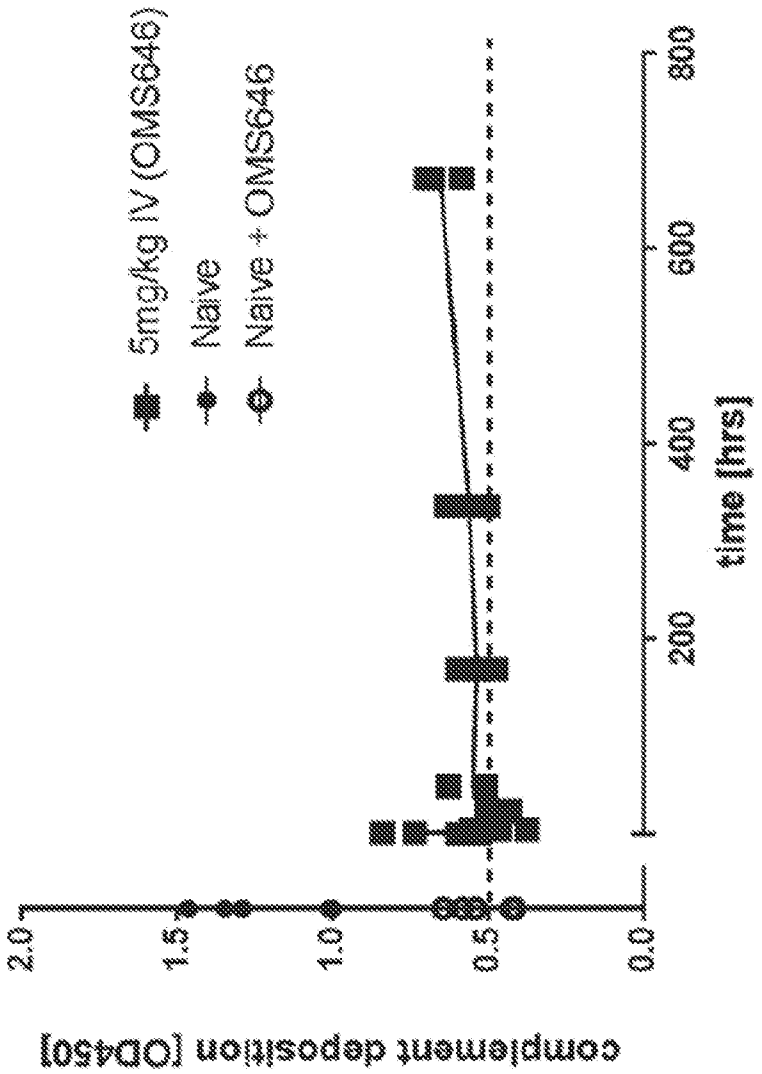

5mg/kg IV (OMS646)
Naive
Naive + OMS646
complement deposition [OD450]
2.0
1.5
1.0
0.5
0.0
200
400
600
800
time [hrs]

FIG. 14A

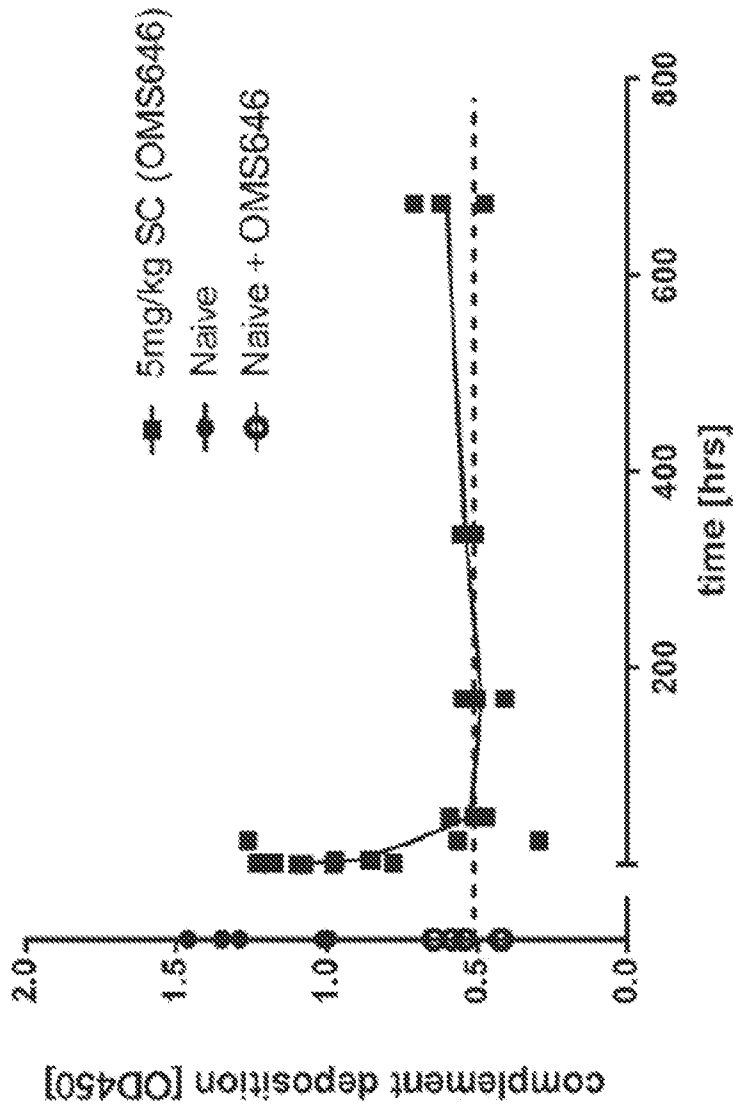

5mg/kg SC (OMS646)
Naive
Naive + OMS646
complement deposition [OD450]
2.0
1.5
1.0
0.5
0.0
200
400
600
800
time [hrs]

FIG. 14B

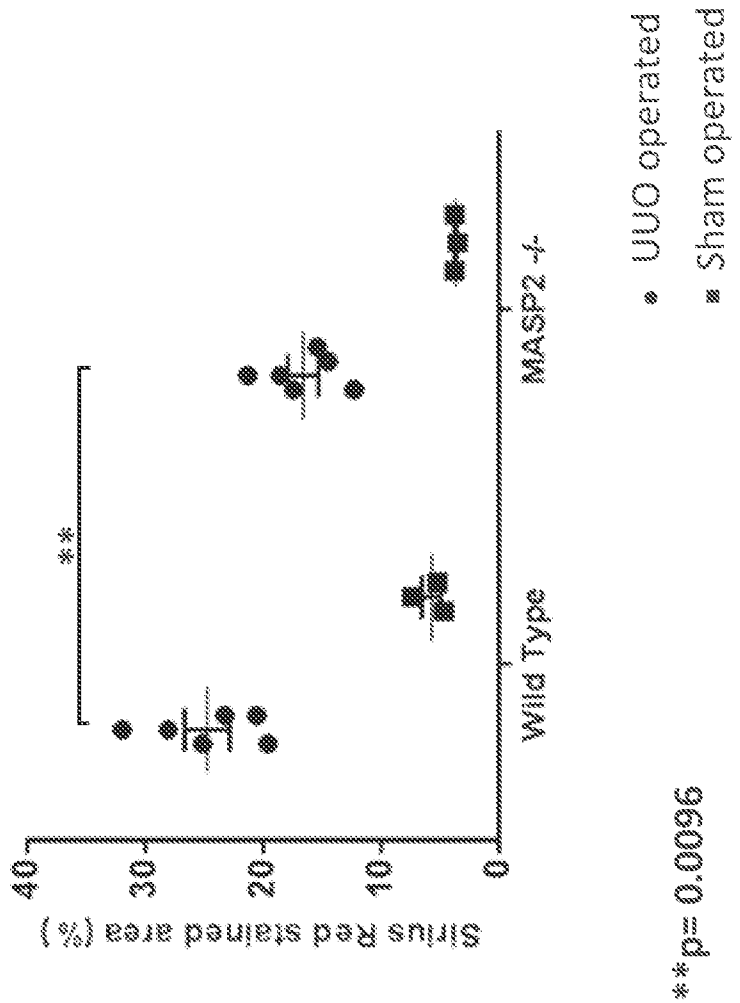

Sirius Red stained area (%)
40
30
20
10
0
**
Wild Type
MASP2 -/-
UUO operated
Sham operated
**p= 0.0096

FIG. 15

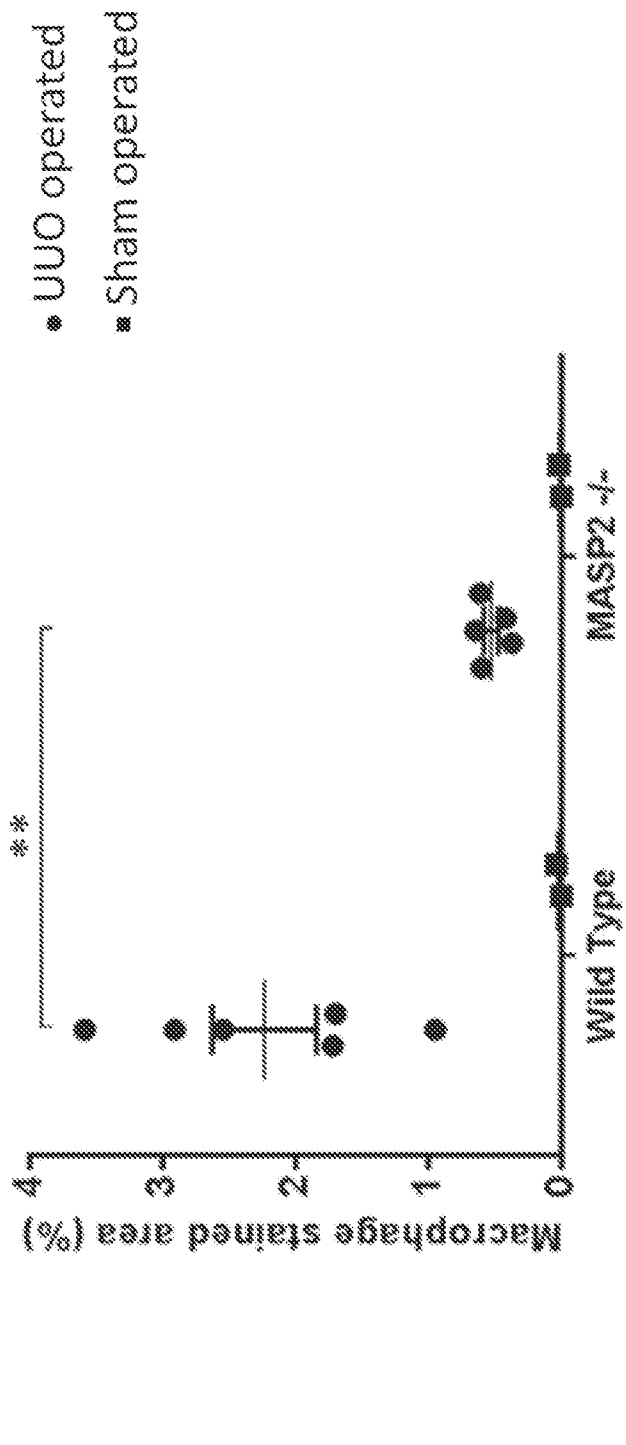

UUO operated
Sham operated
Macrophage stained area (%)
0
1
2
3
4
**
Wild Type
MASP2 -/-
**p=0.0035

FIG. 16

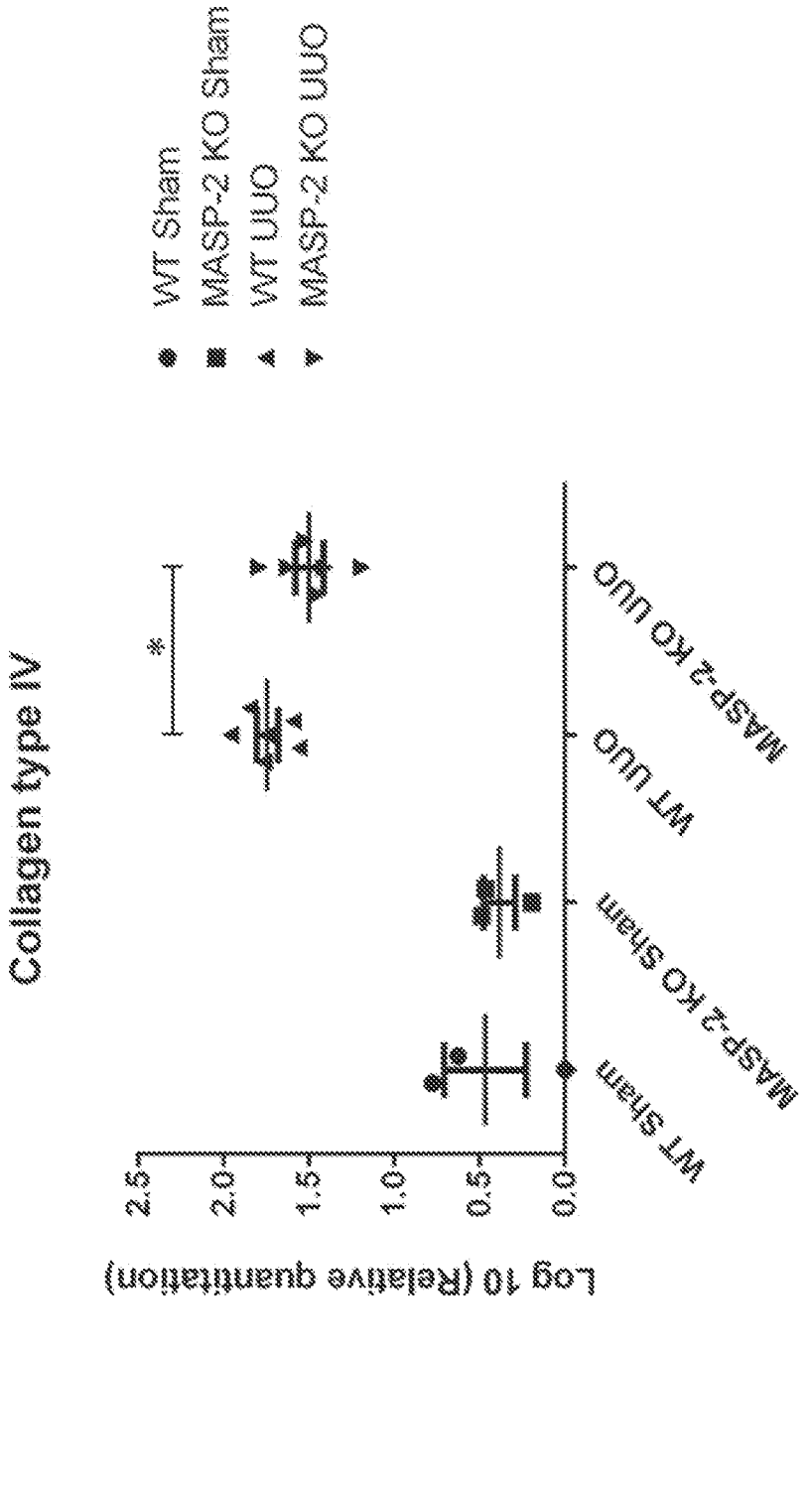

Collagen type IV
Log 10 (Relative quantitation)
2.5
2.0
1.5
1.0
0.5
0.0
*
WT Sham
MASP-2 KO Sham
WT UUO
MASP-2 KO UUO
WT Sham
MASP-2 KO Sham
WT UUO
MASP-2 KO UUO
Mouse group
*p=0.0388

FIG. 17

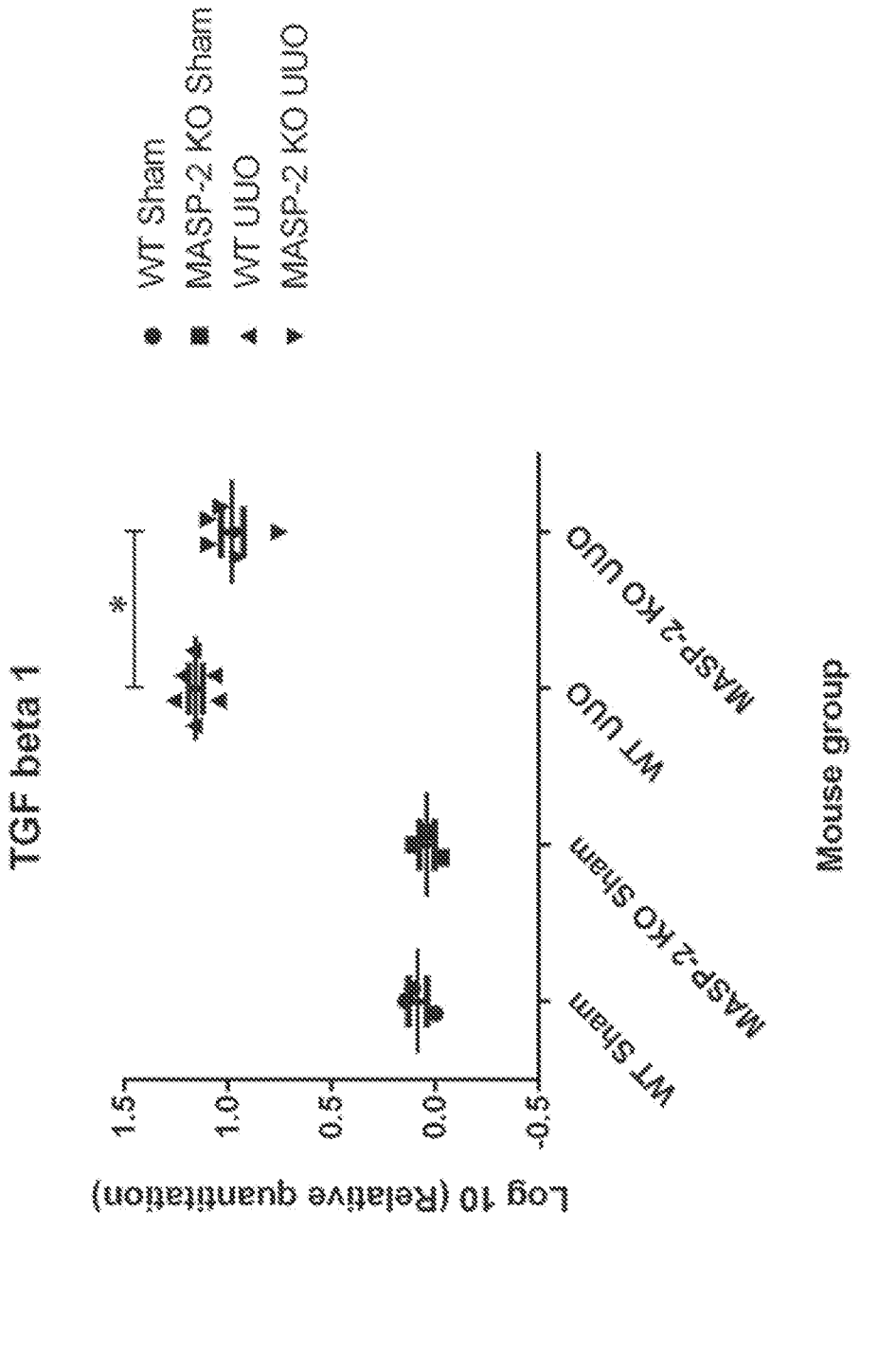

TGF beta 1
WT Sham
MASP-2 KO Sham
WT UUO
MASP-2 KO UUO
*
Log 10 (Relative quantitation)
1.5
1.0
0.5
0.0
-0.5
WT Sham
MASP-2 KO Sham
WT UUO
MASP-2 KO UUO
Mouse group
*p=0.0174

FIG. 18

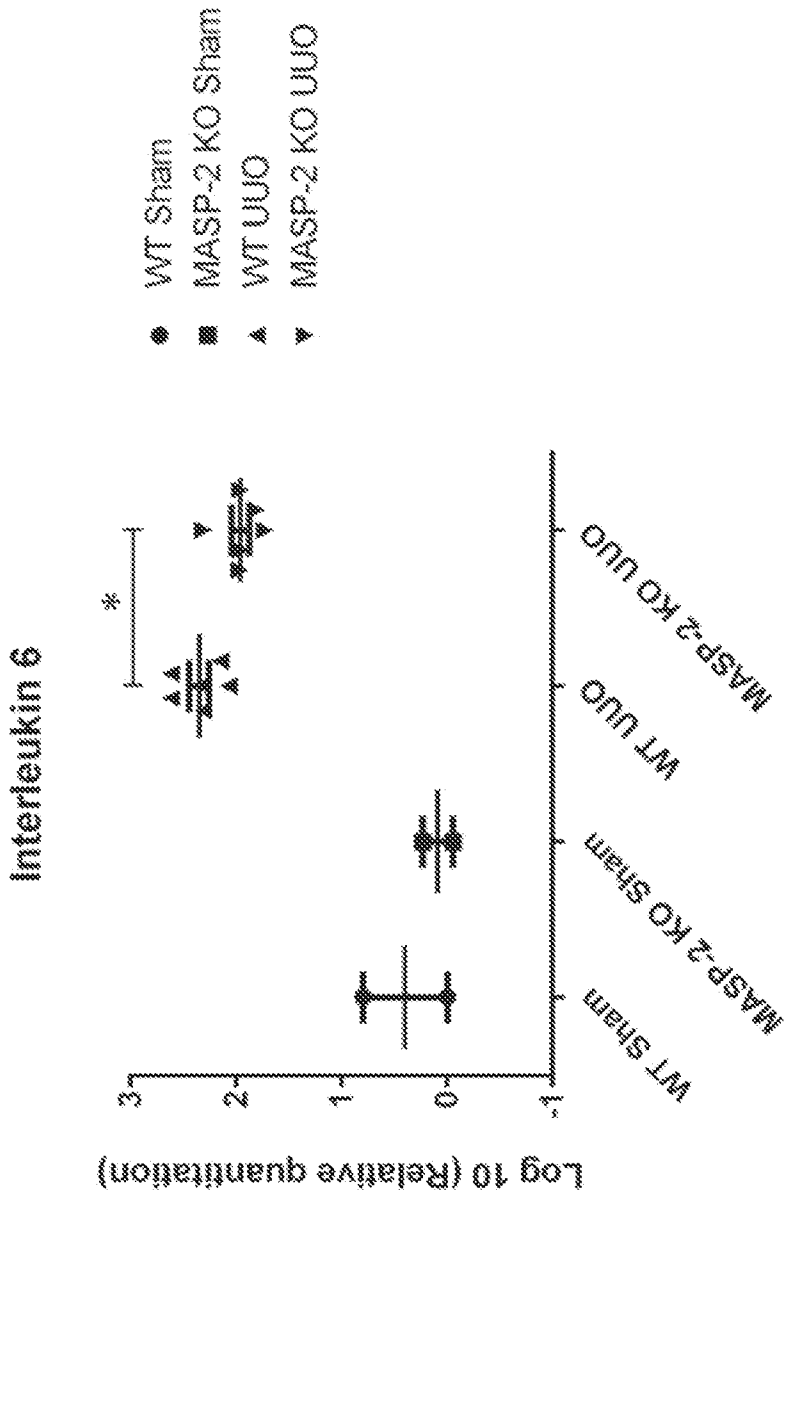

Interleukin 6
Log 10 (Relative quantitation)
5
2
1
0
-1
*
WT Sham
MASP-2 KO Sham
WT UUO
MASP-2 KO UUO
WT Sham
MASP-2 KO Sham
WT UUO
MASP-2 KO UUO
Mouse group
*p=0.0109

FIG. 19

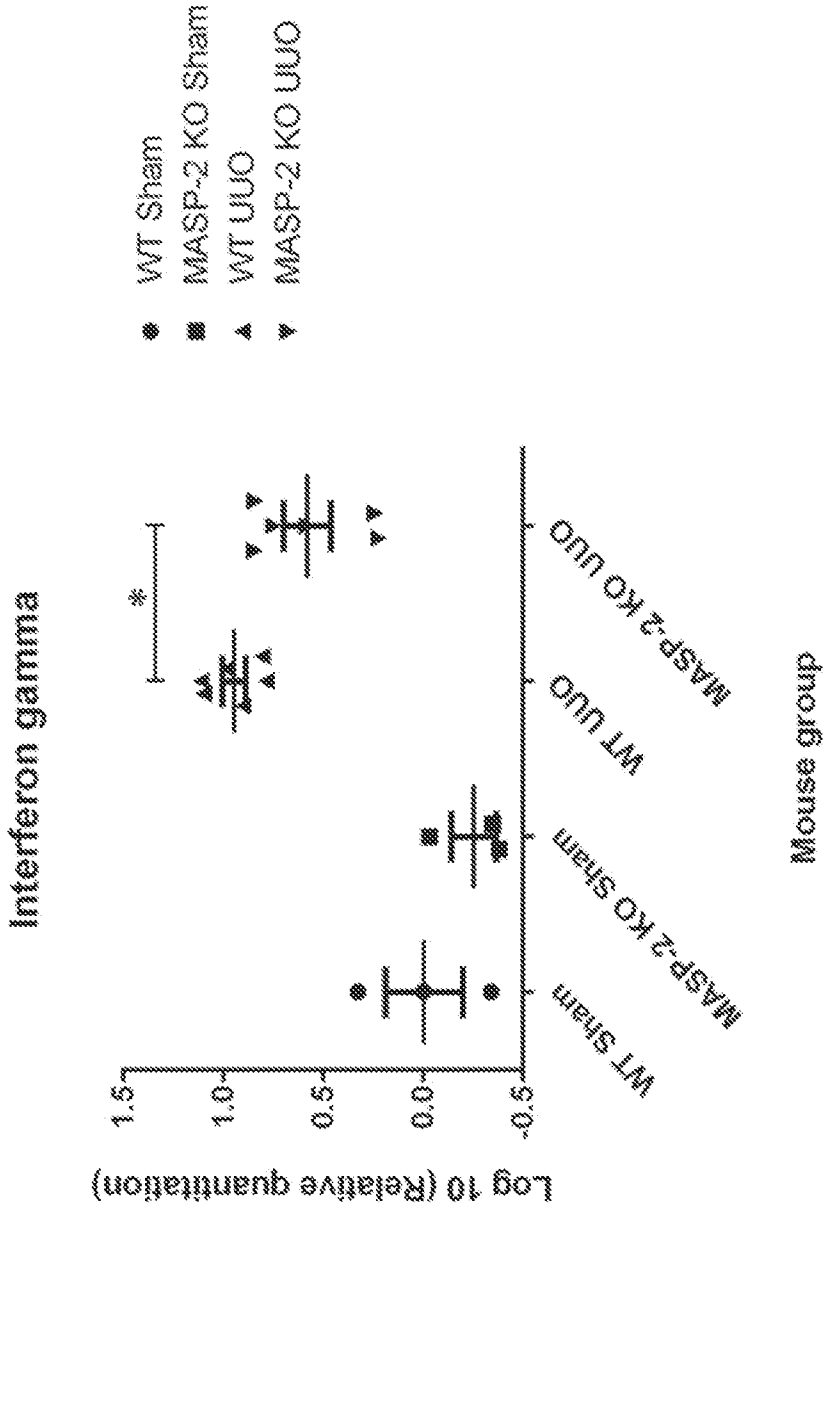

Interferon gamma
WT Sham
MASP-2 KO Sham
WT UUO
MASP-2 KO UUO
*
Log 10 (Relative quantitation)
1.5
1.0
0.5
0.0
-0.5
WT Sham
MASP-2 KO Sham
WT UUO
MASP-2 KO UUO
Mouse group
*p=0.0182

FIG. 20

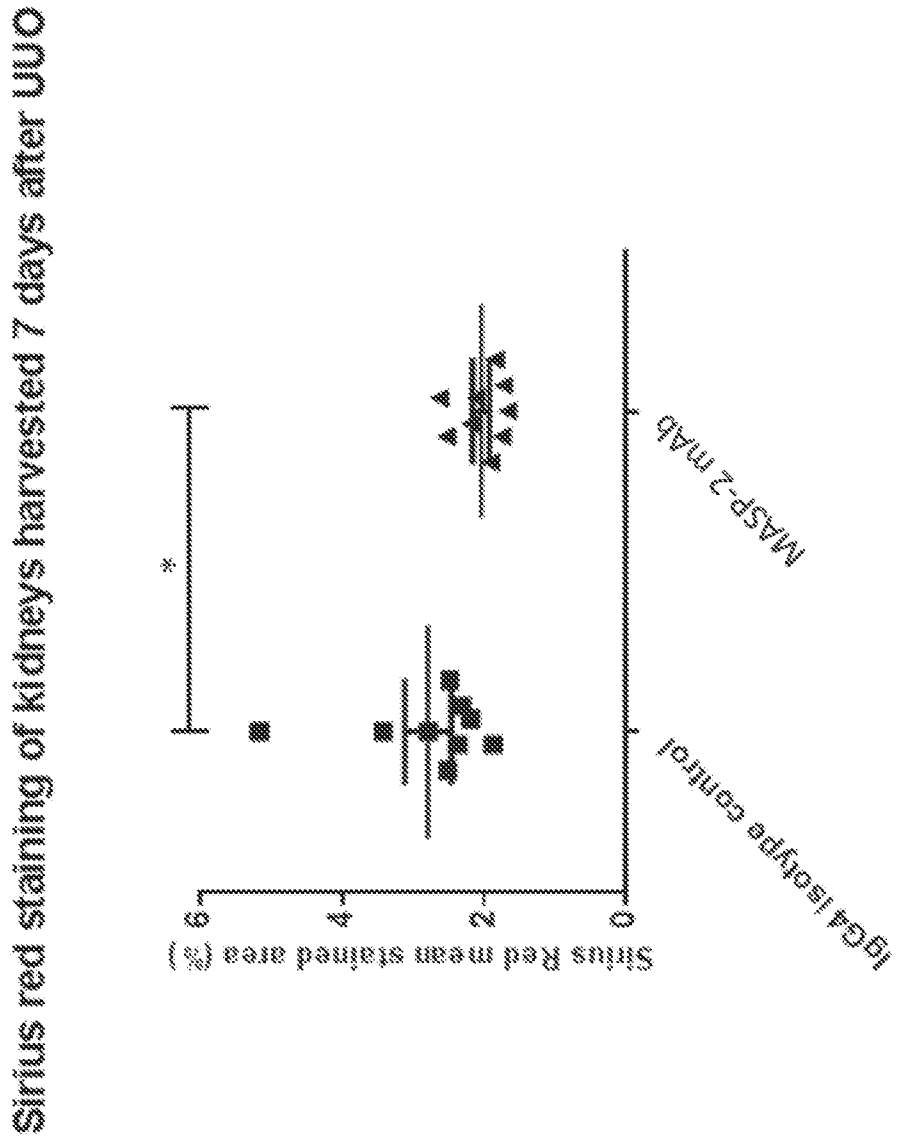

Sirius red staining of kidneys harvested 7 days after UUO
Sirius Red mean stained area (%)
0
2
4
6
*
IgG4 isotype control
MASP-2 mAb
*p=0.0477

FIG. 21

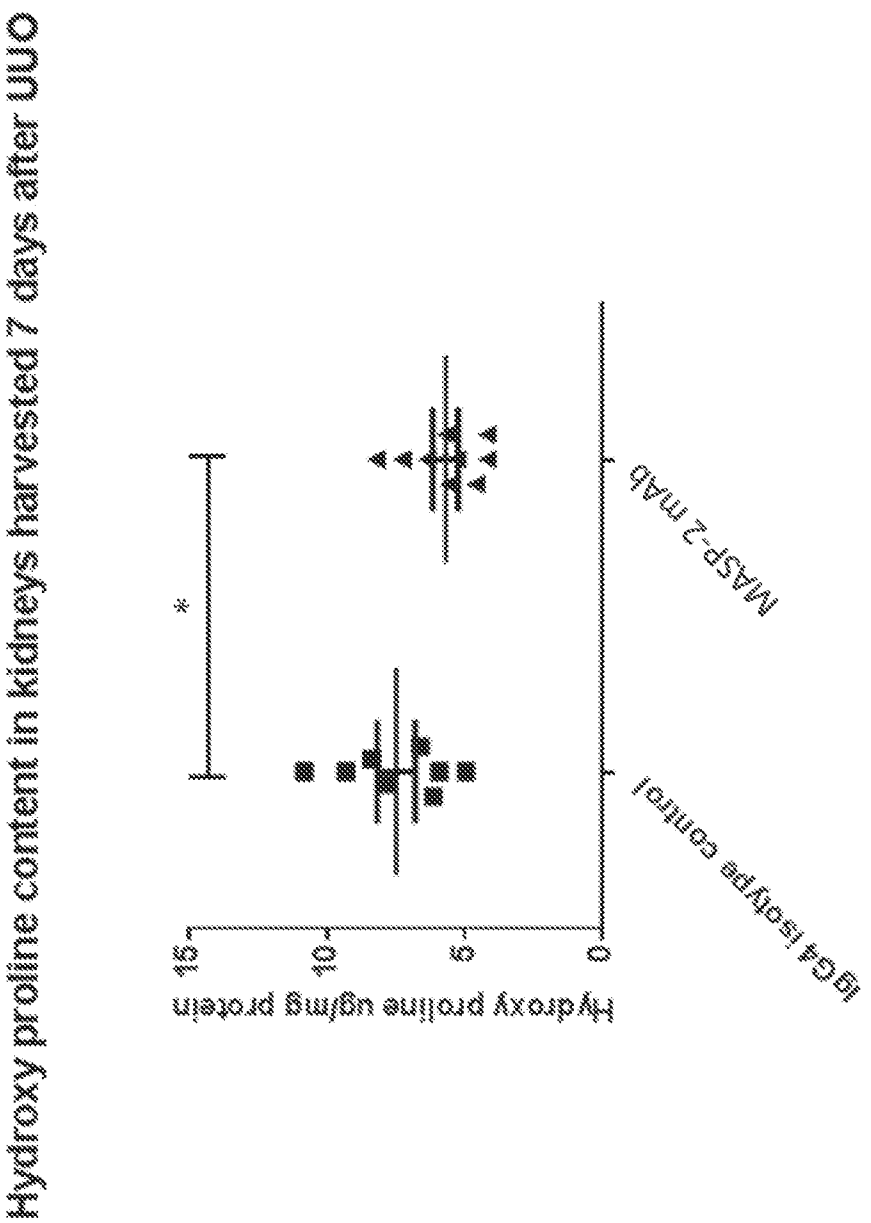

Hydroxy proline content in kidneys harvested 7 days after UUO
Hydroxy proline ug/mg protein
15
10
5
0
*
IgG4 isotype control
MASP-2 mAb
*p=0.0439

FIG. 22

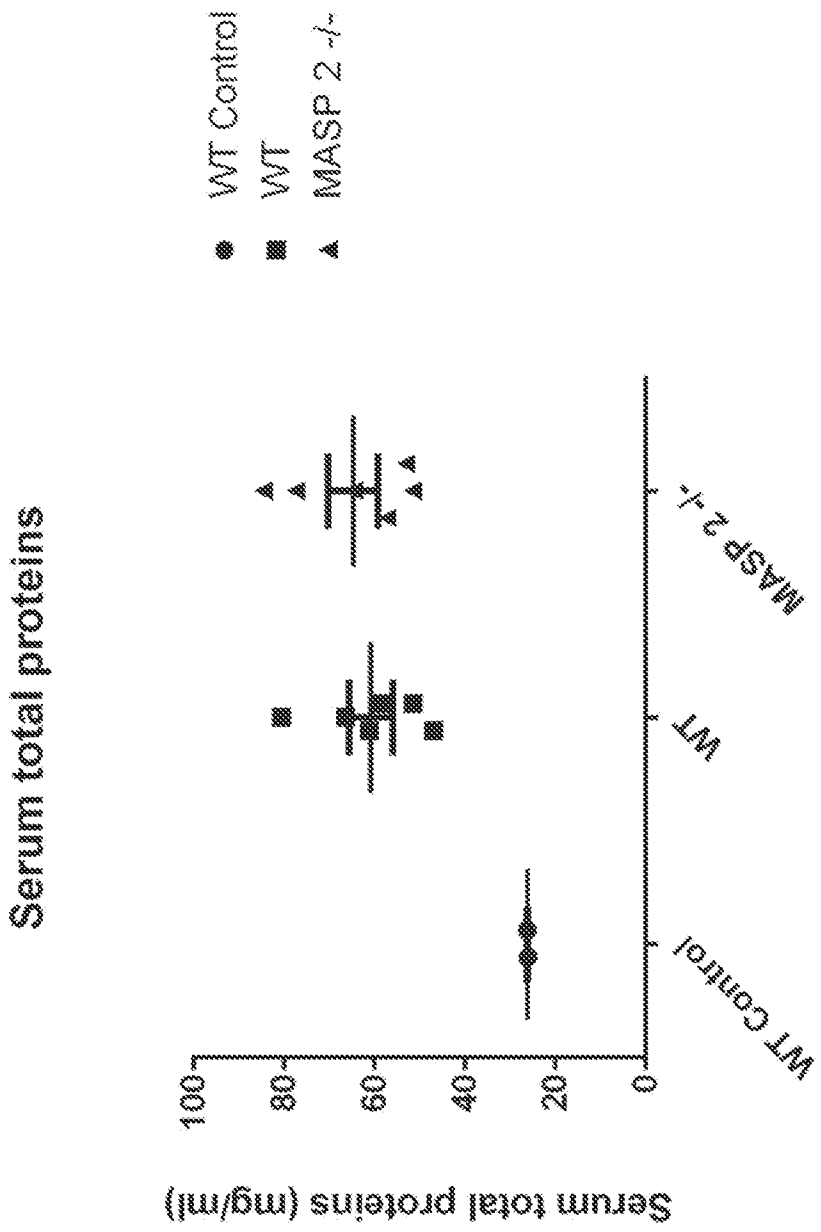

Serum total proteins
WT Control
WT
MASP 2 -/-
100
80
60
40
20
0
Serum total proteins (mg/ml)
WT Control
WT
MASP 2 -/-
Groups

FIG. 23

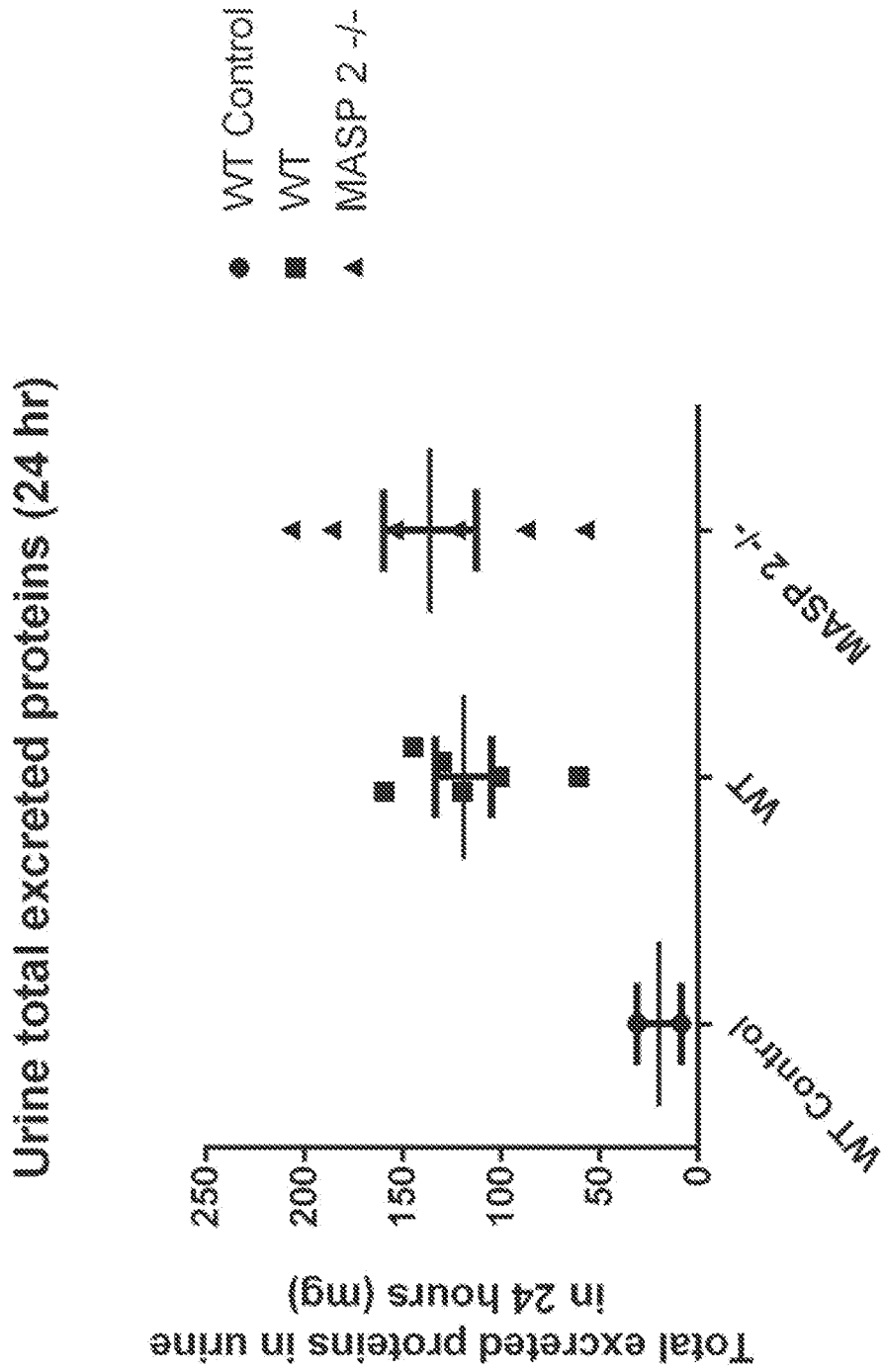

Urine total excreted proteins (24 hr)
WT Control
WT
MASP 2 -/-
Total excreted proteins in urine in 24 hours (mg)
250
200
150
100
50
0
WT Control
WT
MASP 2 -/-
Groups

FIG. 24

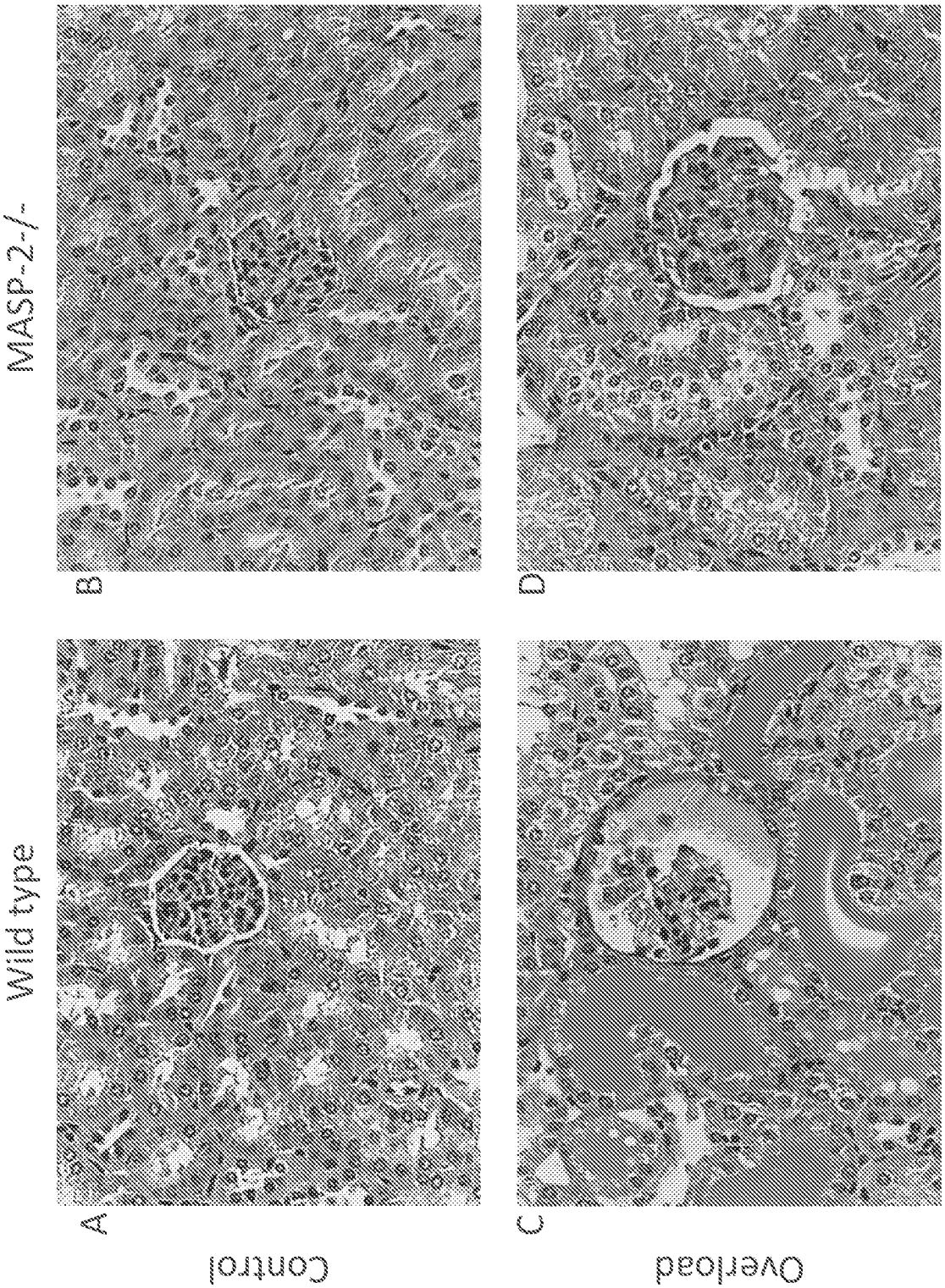


FIG. 25

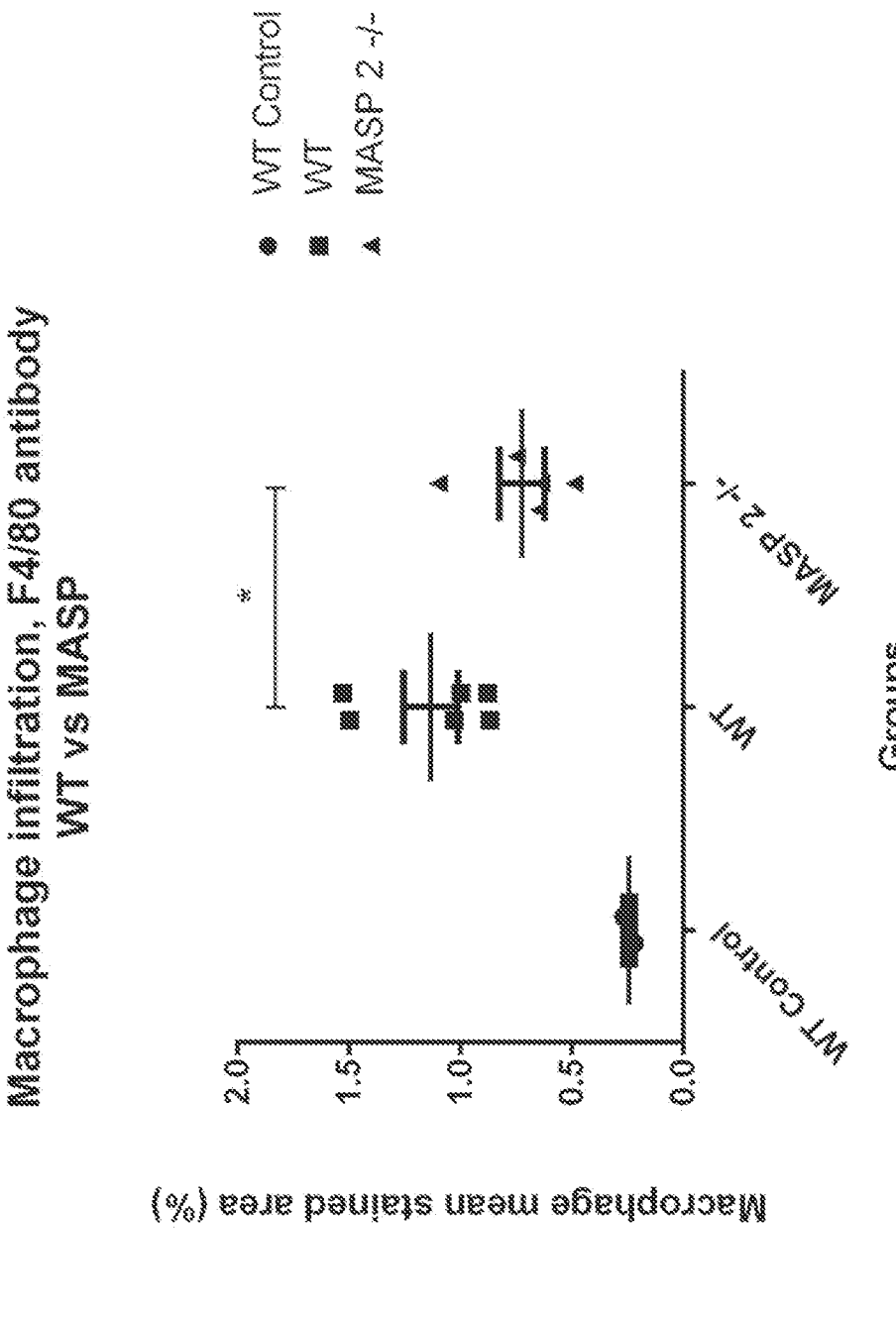

Macrophage infiltration, F4/80 antibody
WT vs MASP
WT Control
WT
MASP 2 -/-
*
2.0
1.5
1.0
0.5
0.0
Macrophage mean stained area (%)
WT Control
WT
MASP 2 -/-
Groups
*p=0.035

FIG. 26

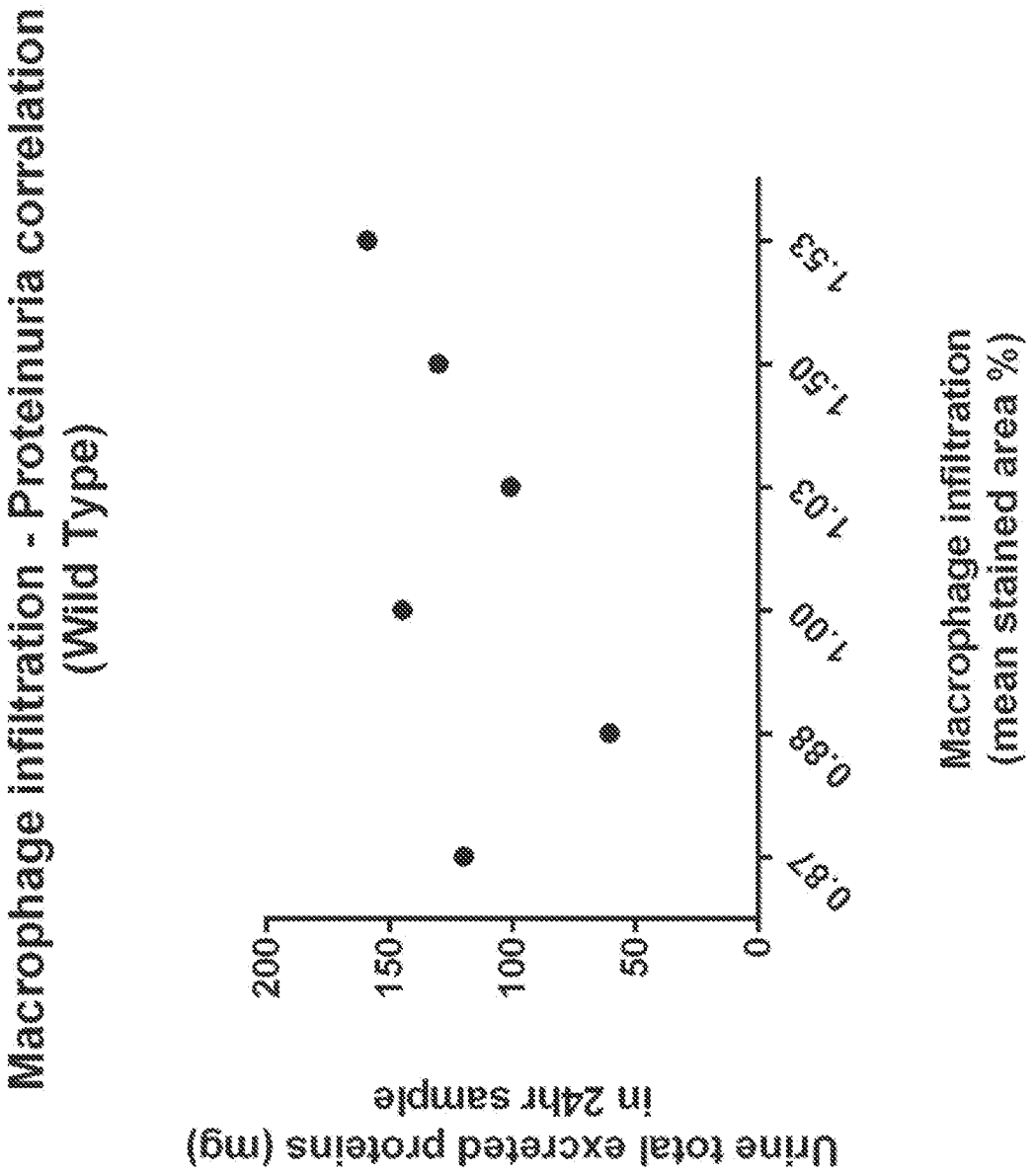

Macrophage infiltration - Proteinuria correlation
(Wild Type)
Urine total excreted proteins (mg)
in 24hr sample
200
150
100
50
0
0.87
0.88
1.00
1.03
1.50
1.53
Macrophage infiltration
(mean stained area %)

FIG. 27A

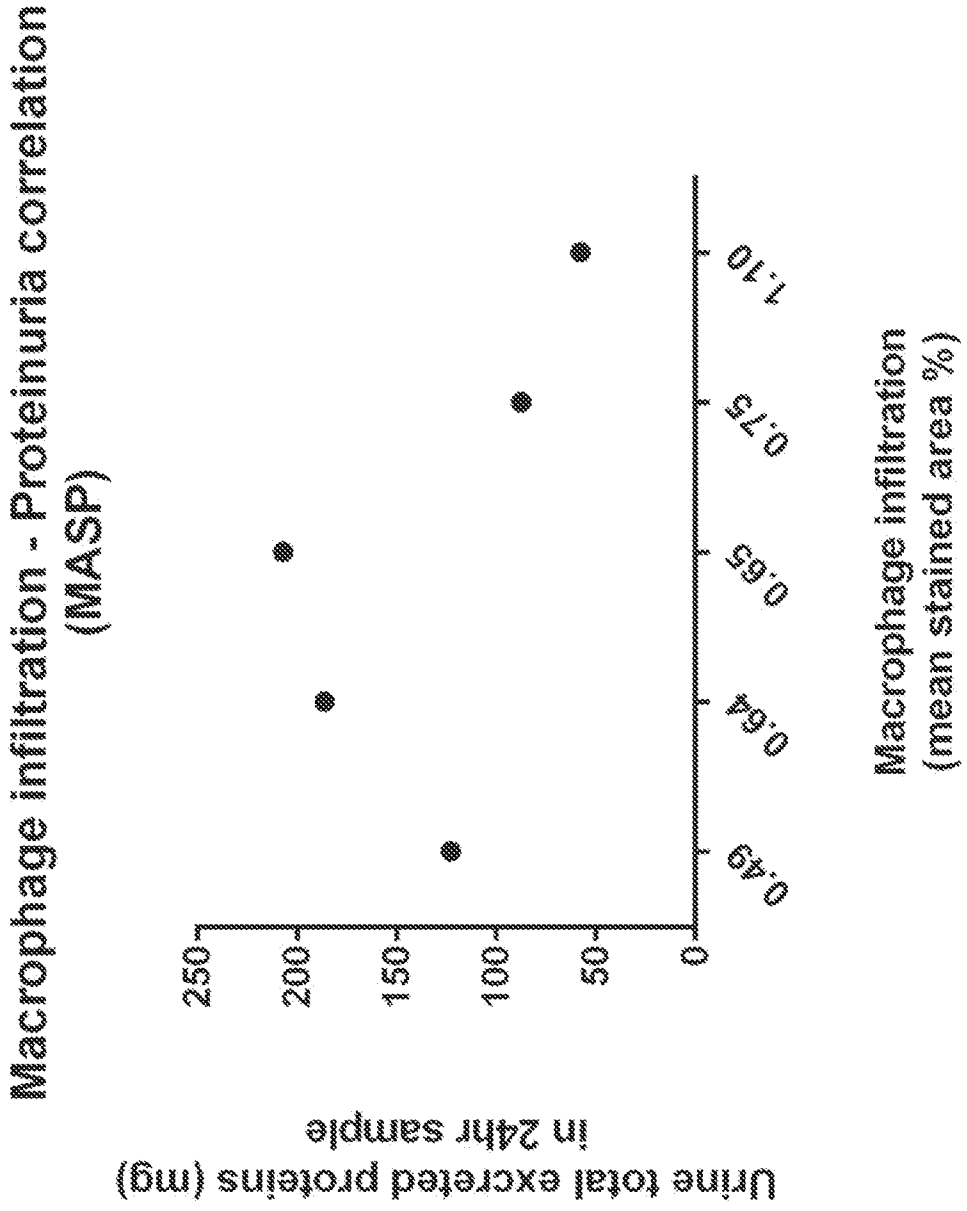

Macrophage infiltration - Proteinuria correlation
(MASP)
Urine total excreted proteins (mg)
in 24hr sample
250
200
150
100
50
0
0.49
0.64
0.65
0.75
1.10
Macrophage infiltration
(mean stained area %)

FIG. 27B

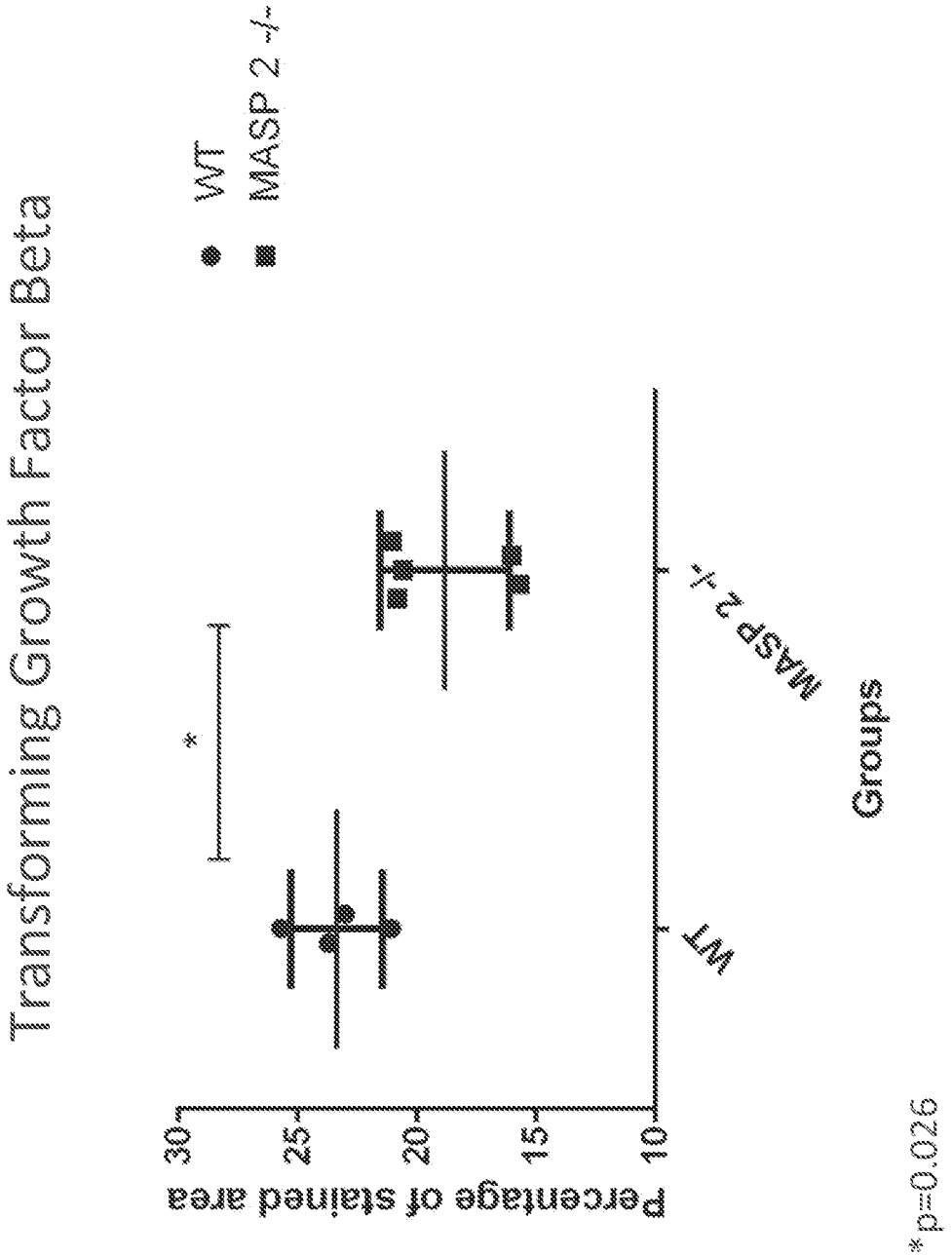

Transforming Growth Factor Beta
WT
MASP 2 -/-
*
Percentage of stained area
30
25
20
15
10
WT
MASP 2 -/-
Groups
* p=0.026

FIG. 28

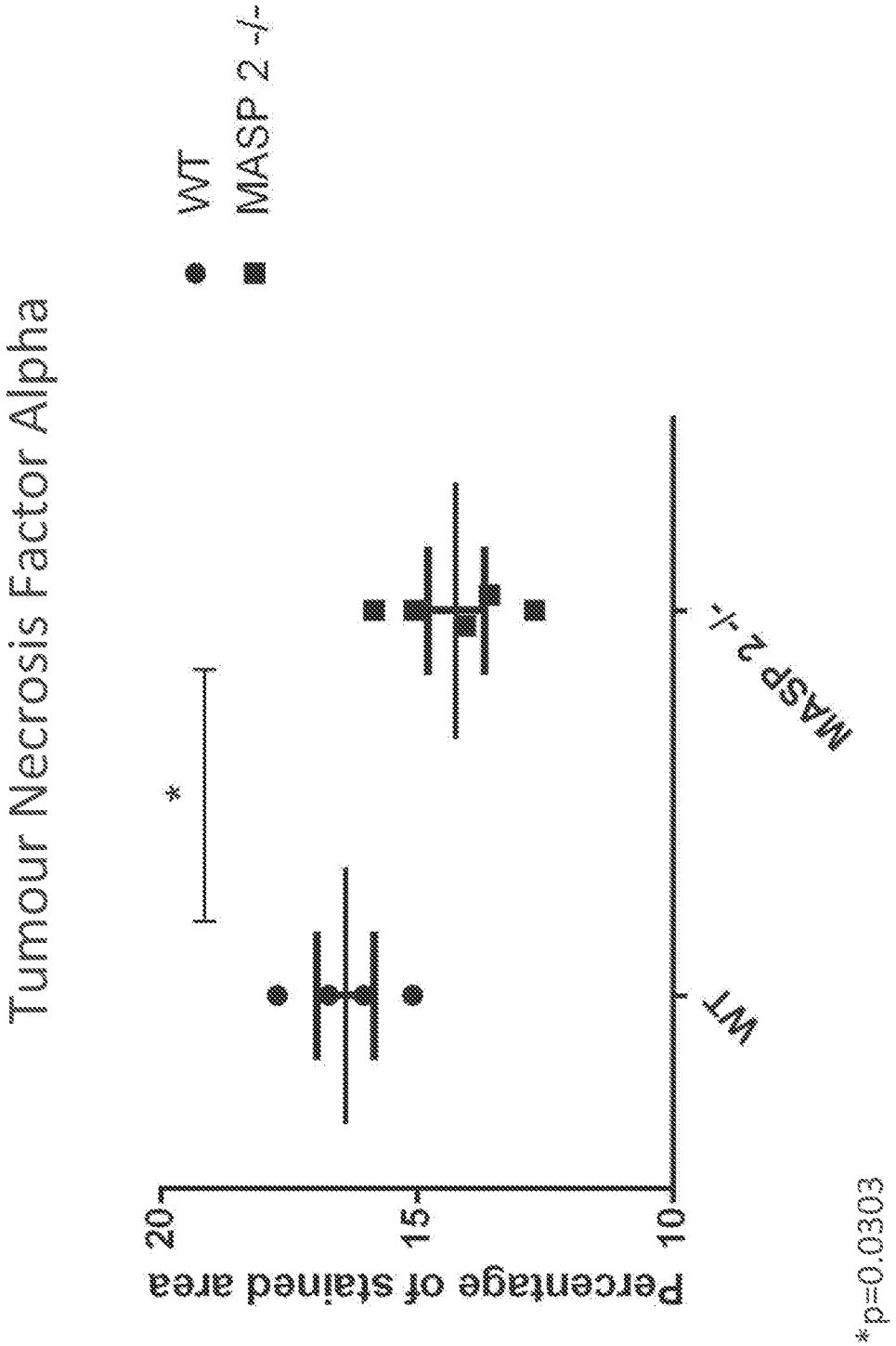

Tumour Necrosis Factor Alpha
WT
MASP 2 -/-
*
Percentage of stained area
20
15
10
WT
MASP 2 -/-
*p=0.0303

FIG. 29

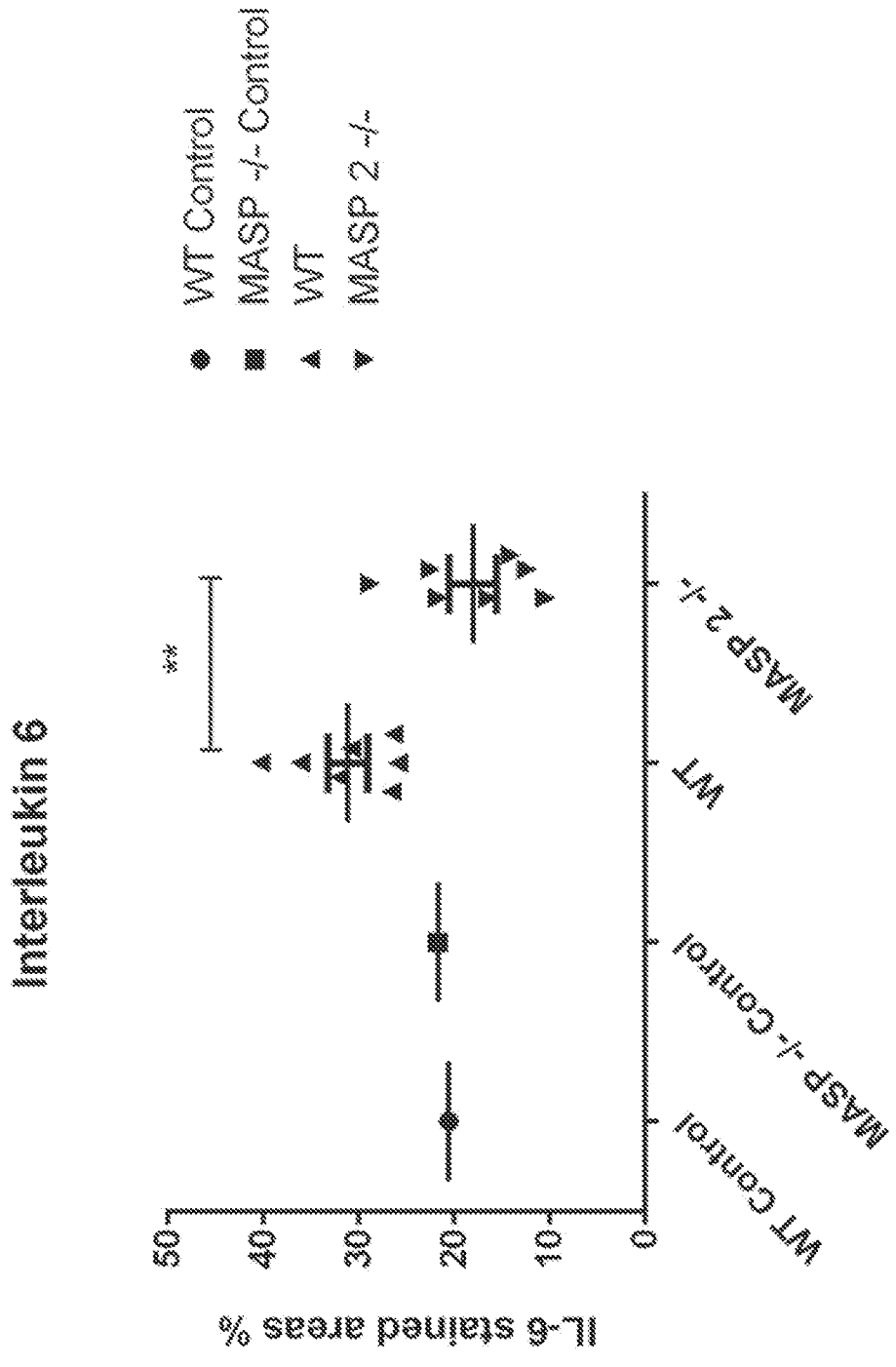

Interleukin 6
WT Control
MASP -/- Control
WT
MASP 2 -/-
**
IL-6 stained areas %
50
40
30
20
10
0
WT Control
MASP -/- Control
WT
MASP 2 -/-
Groups
**p=0.0016

FIG. 30

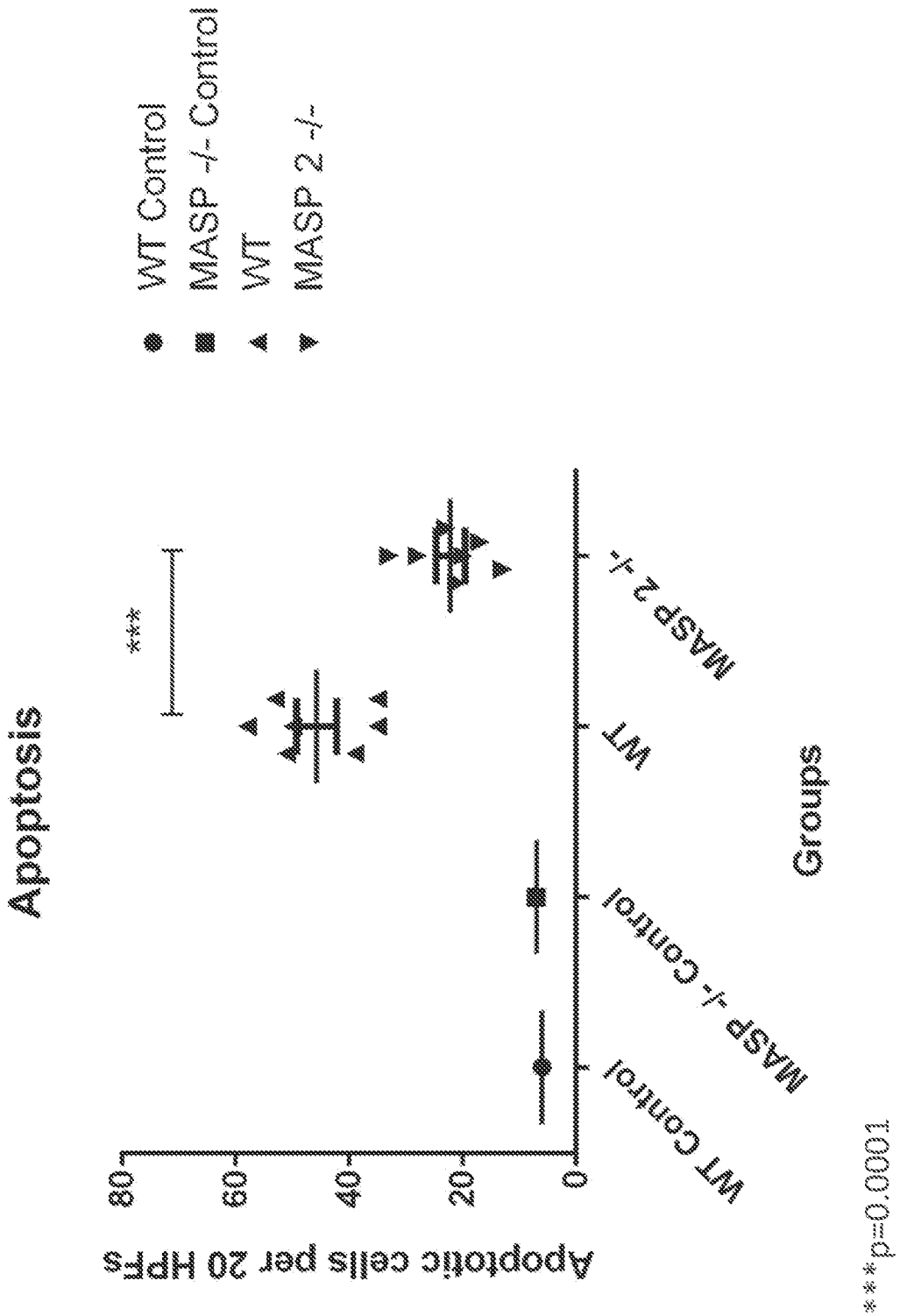

Apoptosis
WT Control
MASP -/- Control
WT
MASP 2 -/-
***
Apoptotic cells per 20 HPFs
0
20
40
60
80
WT Control
MASP -/- Control
WT
MASP 2 -/-
Groups
***p=0.0001

FIG. 31

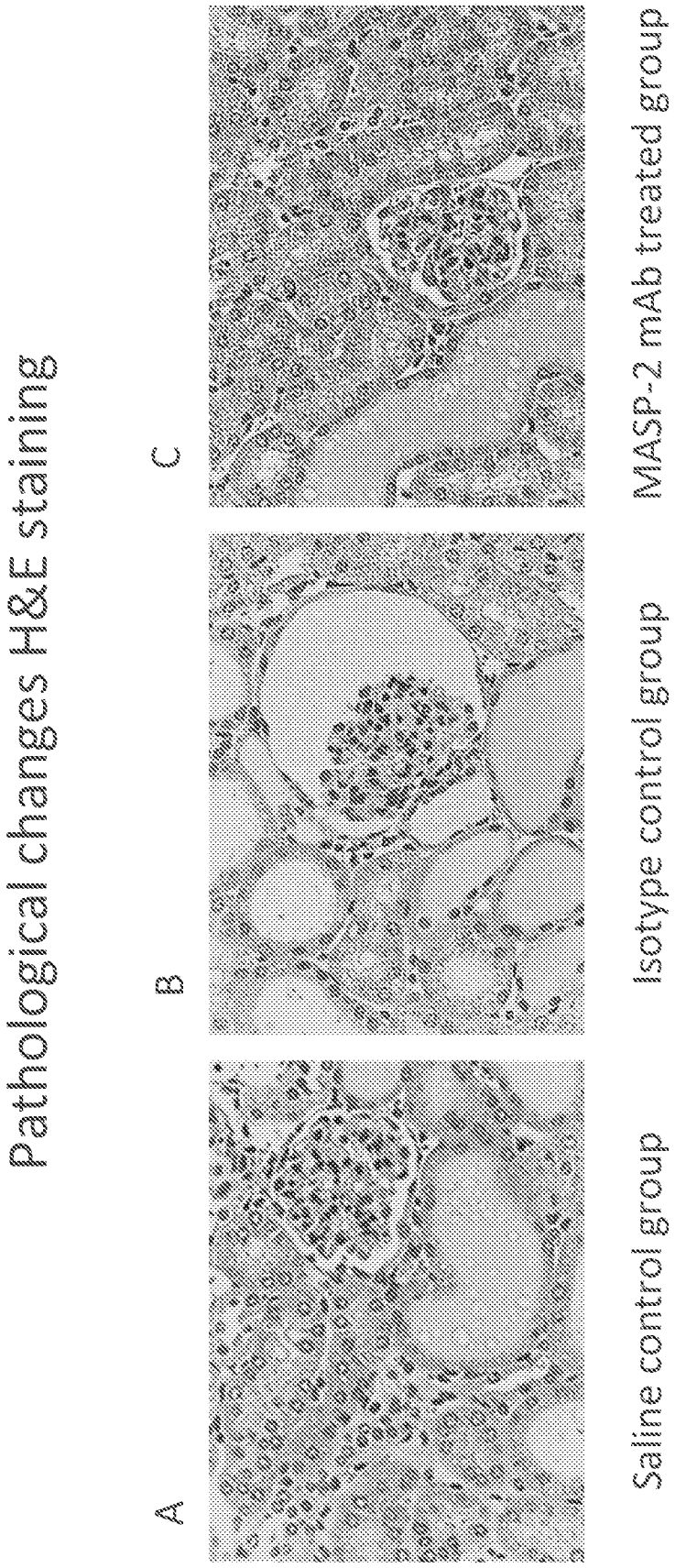

Pathological changes H&E staining
A
B
C
Saline control group
Isotype control group
MASP-2 mAb treated group

FIG. 32

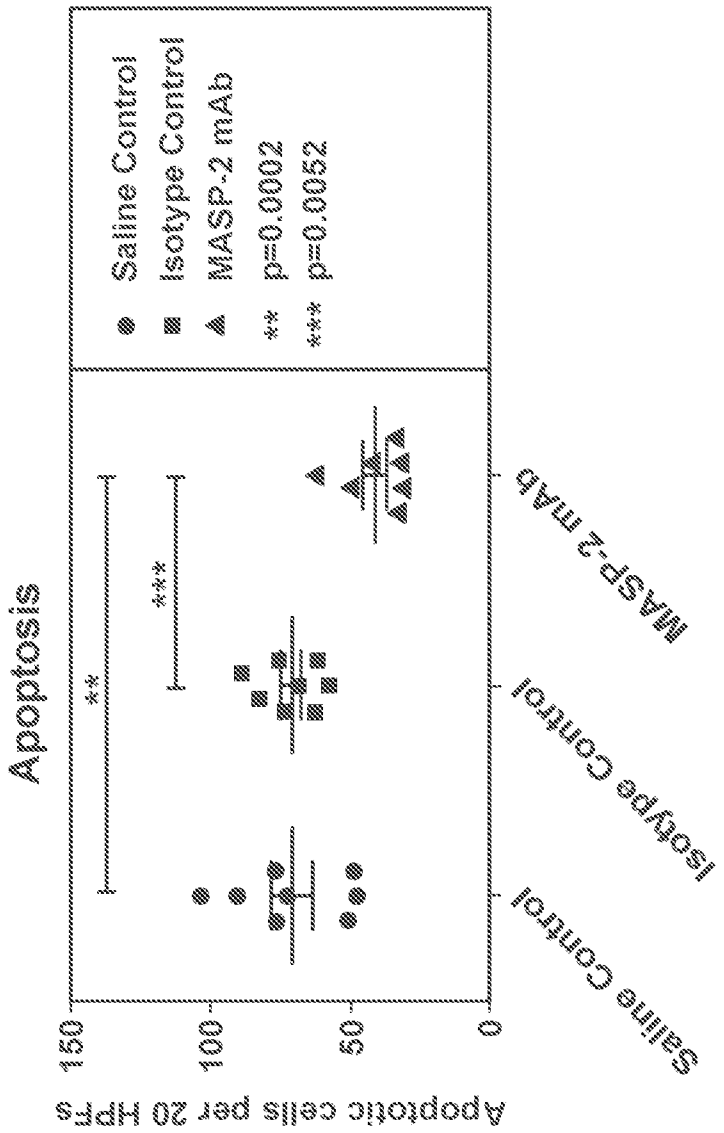

Apoptosis
Saline Control
Isotype Control
MASP-2 mAb
** p=0.0002
*** p=0.0052
**
***
150
100
50
0
Apoptotic cells per 20 HPFs
Saline Control
Isotype Control
MASP-2 mAb
Groups

FIG. 33

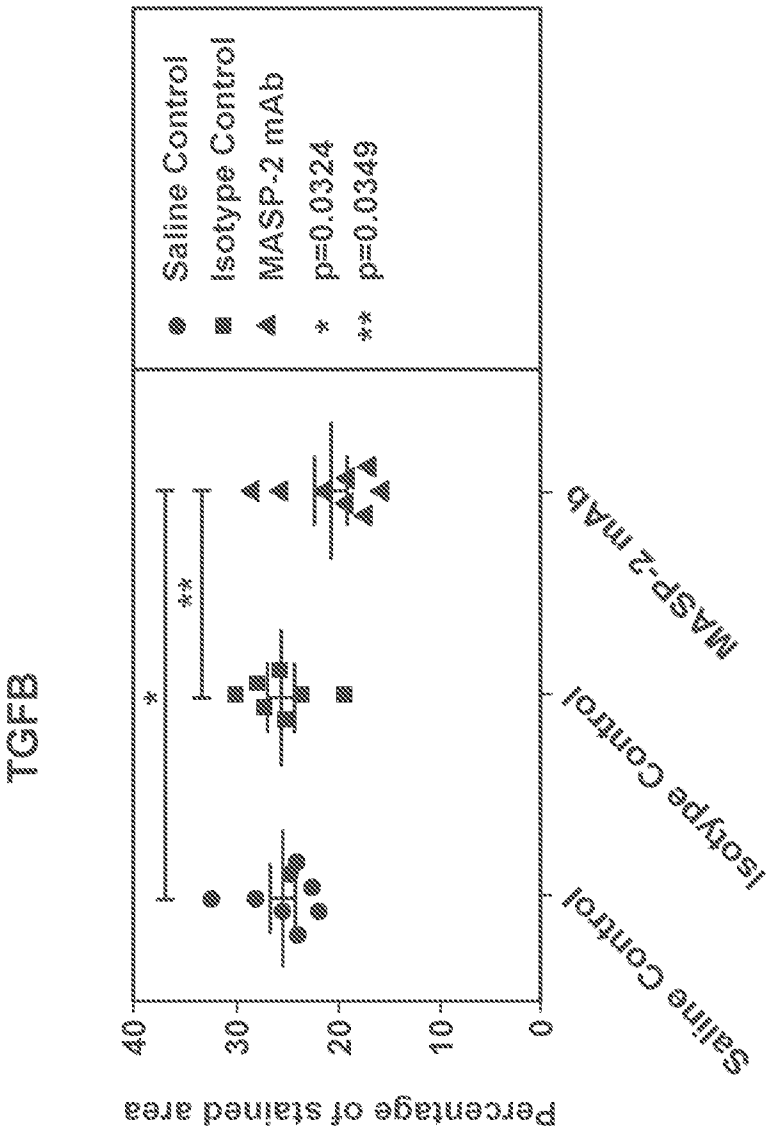

TGFB
Saline Control
Isotype Control
MASP-2 mAb
* p=0.0324
** p=0.0349
Percentage of stained area
0
10
20
30
40
*
**
Saline Control
Isotype Control
MASP-2 mAb
Groups

FIG. 34

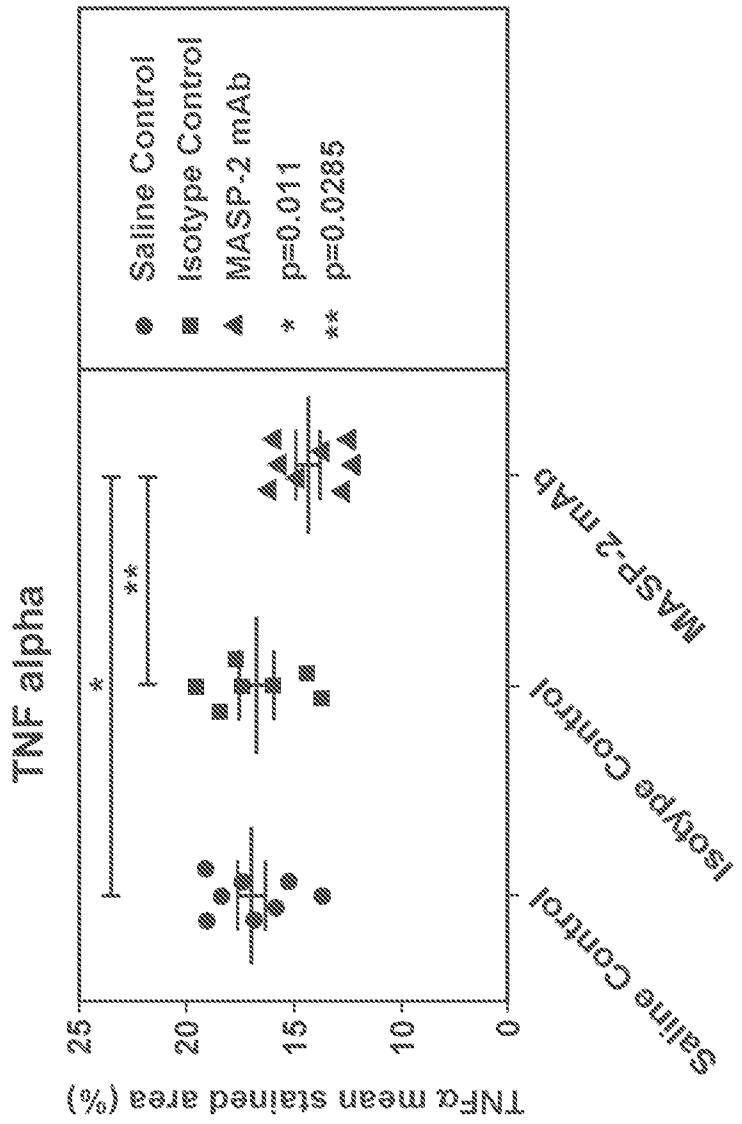

TNF alpha
Saline Control
Isotype Control
MASP-2 mAb
* p=0.011
** p=0.0285
TNFα mean stained area (%)
0
10
15
20
25
Saline Control
Isotype Control
MASP-2 mAb
Mouse Groups

FIG. 35

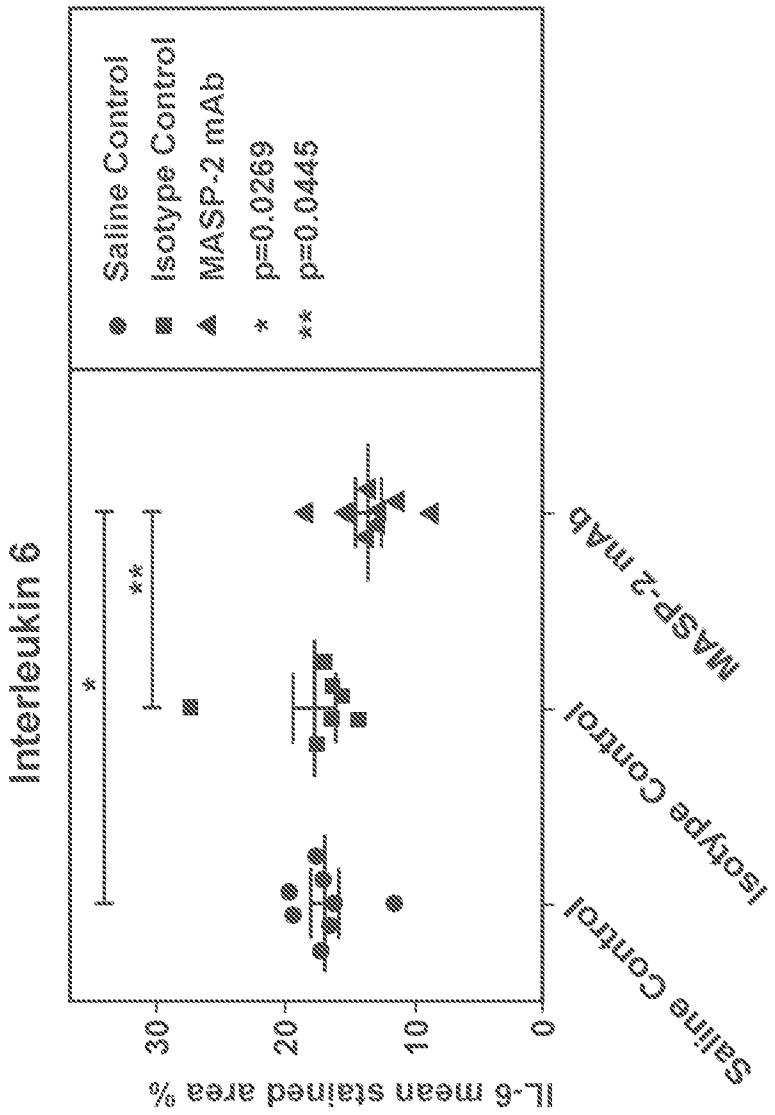

Interleukin 6
Saline Control
Isotype Control
MASP-2 mAb
* p=0.0269
** p=0.0445
IL-6 mean stained area %
0
10
20
30
*
**
Saline Control
Isotype Control
MASP-2 mAb
Mouse Groups

FIG. 36

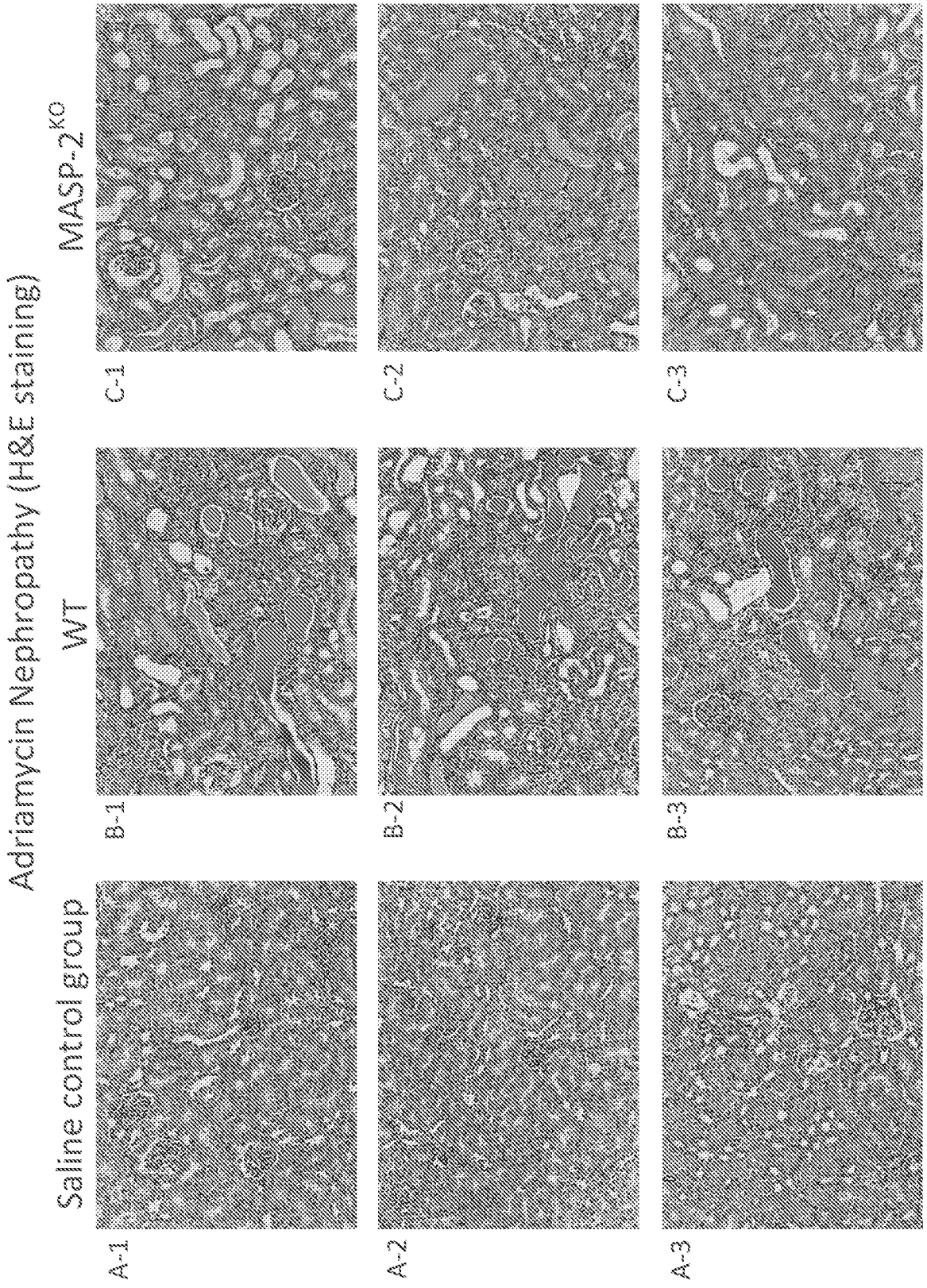

Adriamycin Nephropathy (H&E staining)
Saline control group
WT
MASP-2KO
A-1
A-2
A-3
B-1
B-2
B-3
C-1
C-2
C-3

FIG. 37

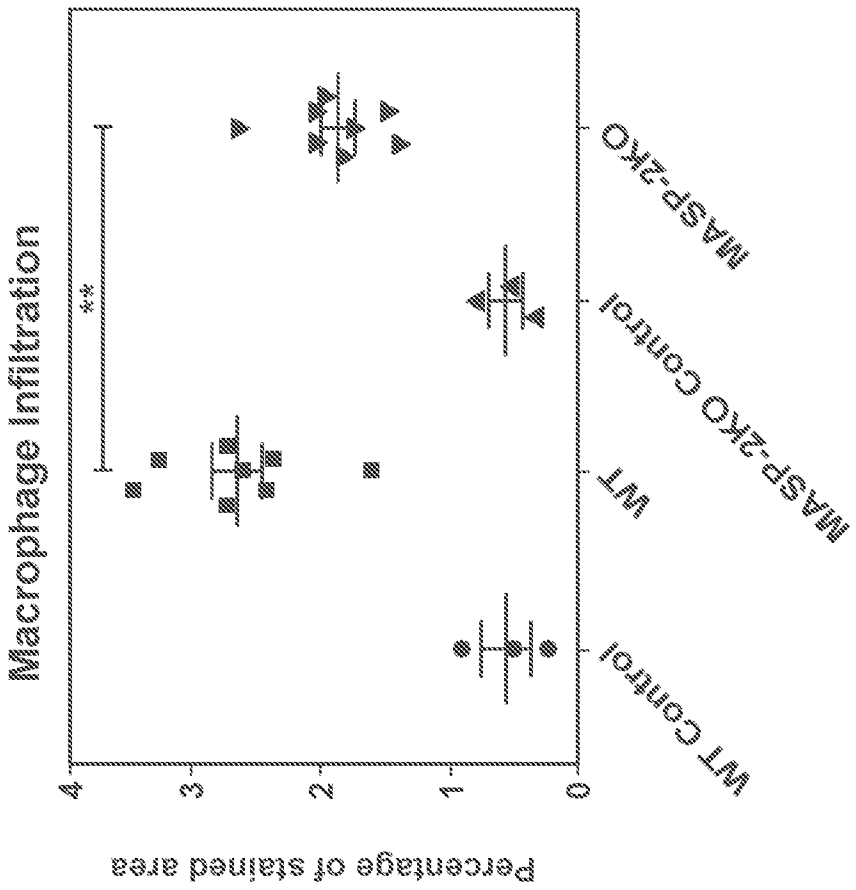

Macrophage Infiltration
Percentage of stained area
0
1
2
3
4
**
WT Control
WT
MASP-2KO Control
MASP-2KO

FIG. 38

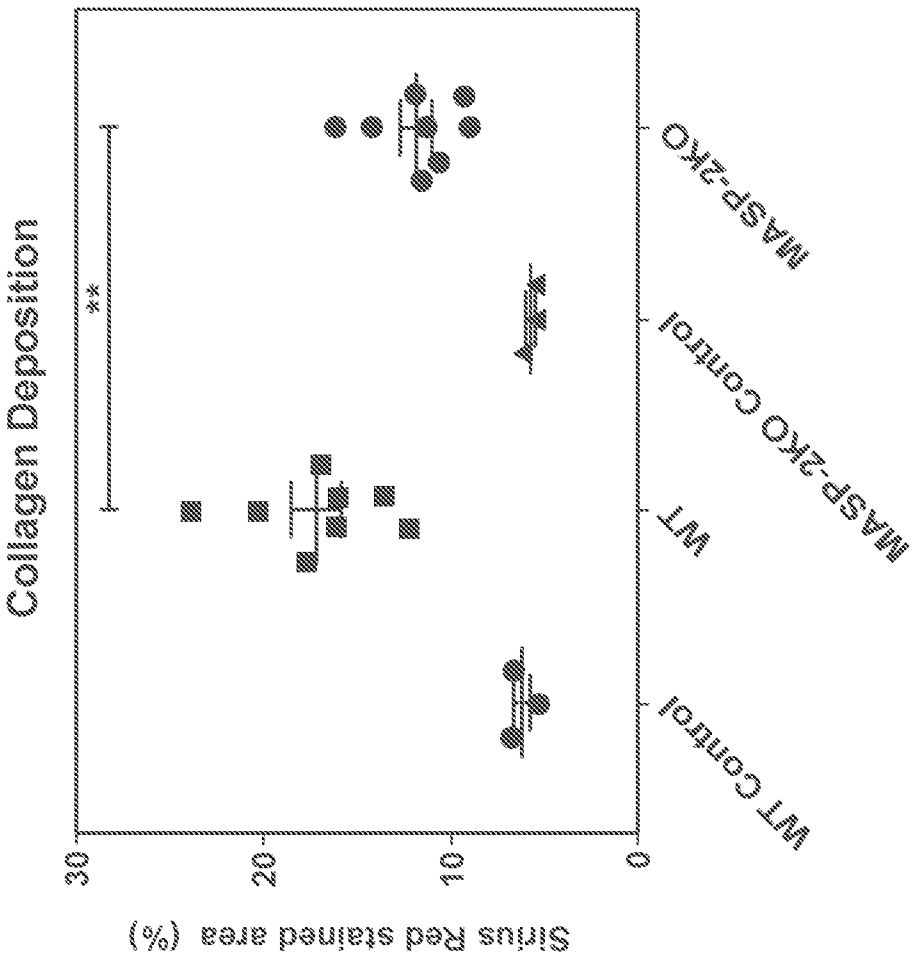

Collagen Deposition
Sirius Red stained area (%)
0
10
20
30
**
WT Control
WT
MASP-2KO Control
MASP-2KO

FIG. 39

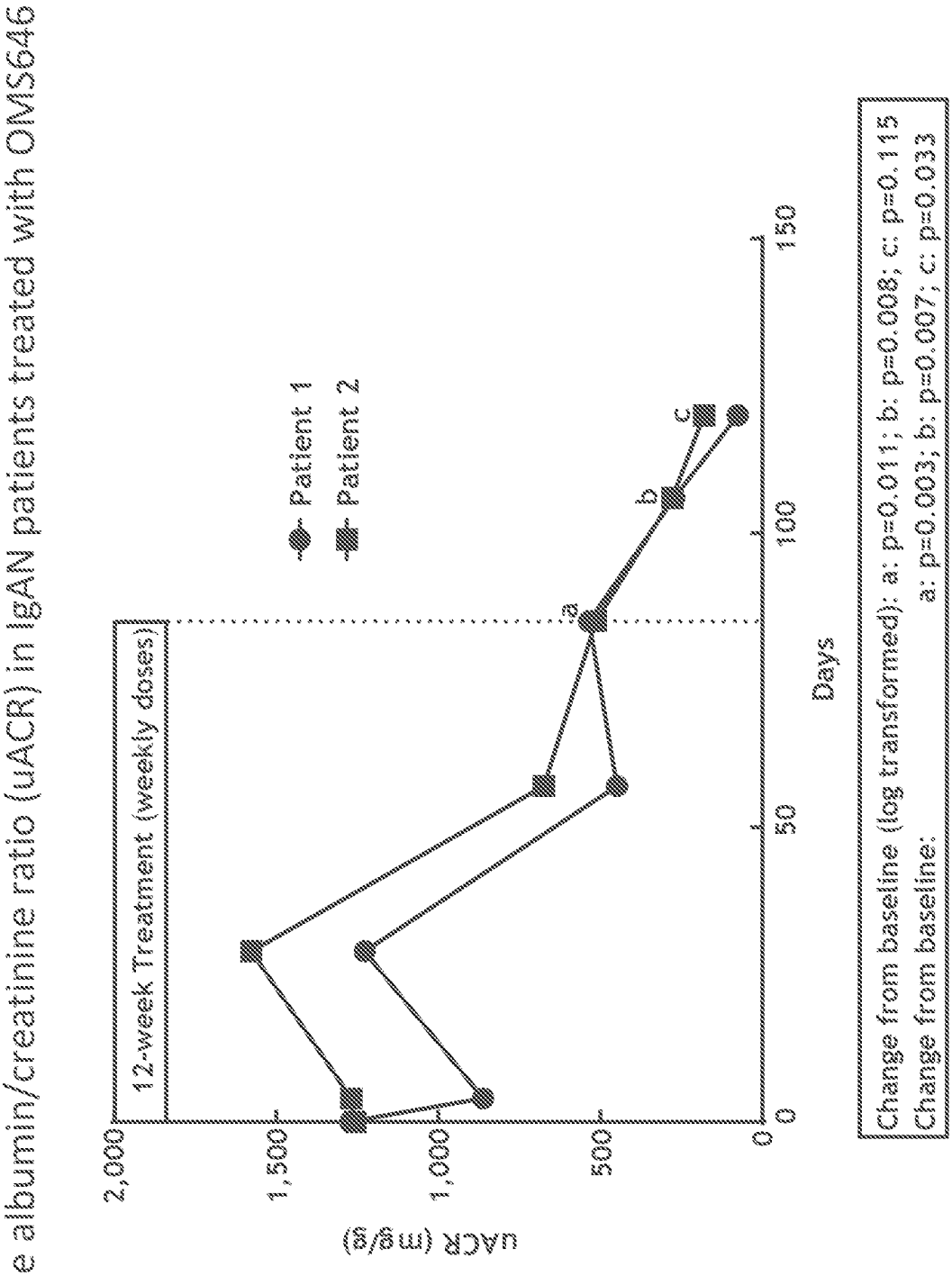

Urine albumin/creatinine ratio (uACR) in IgAN patients treated with OMS646
12-week Treatment (weekly doses)
Patient 1
Patient 2
uACR (mg/g)
2,000
1,500
1,000
500
0
0
50
100
150
Days
a
b
c
Change from baseline (log transformed): a: p=0.011; b: p=0.008; c: p=0.115
Change from baseline: a: p=0.003; b: p=0.007; c: p=0.033

FIG. 40

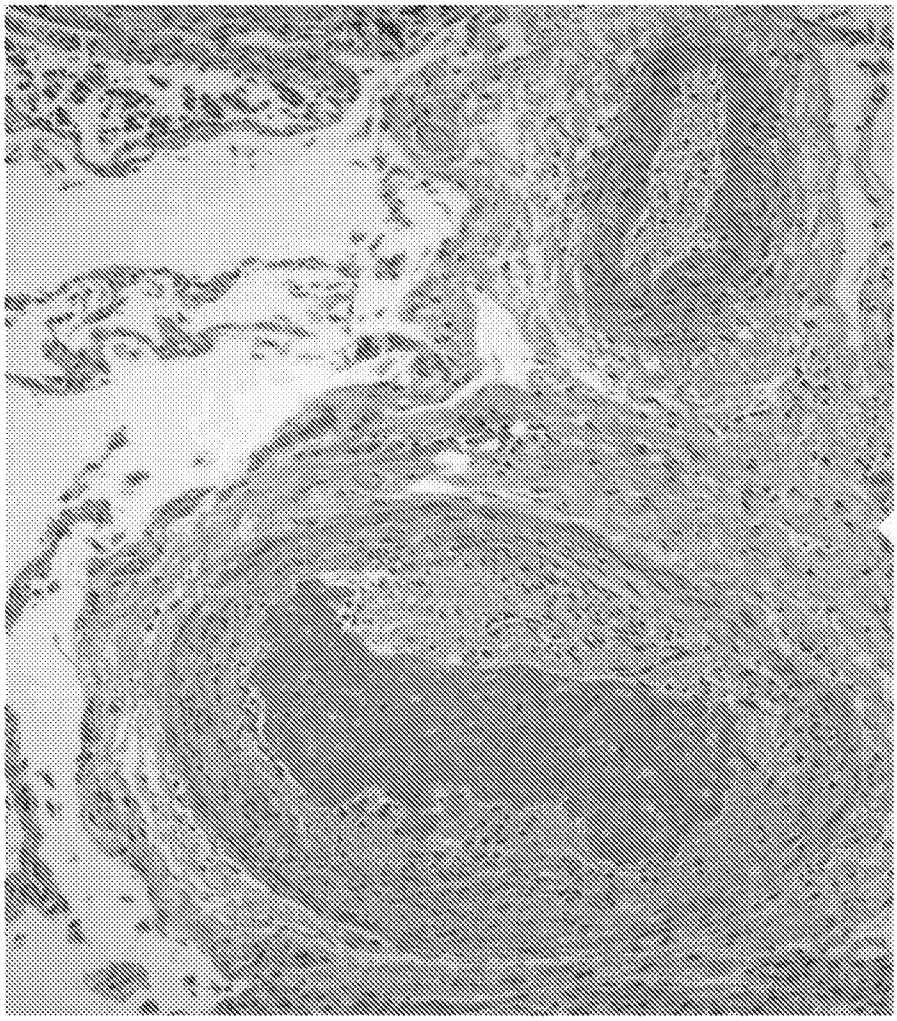


FIG. 41A

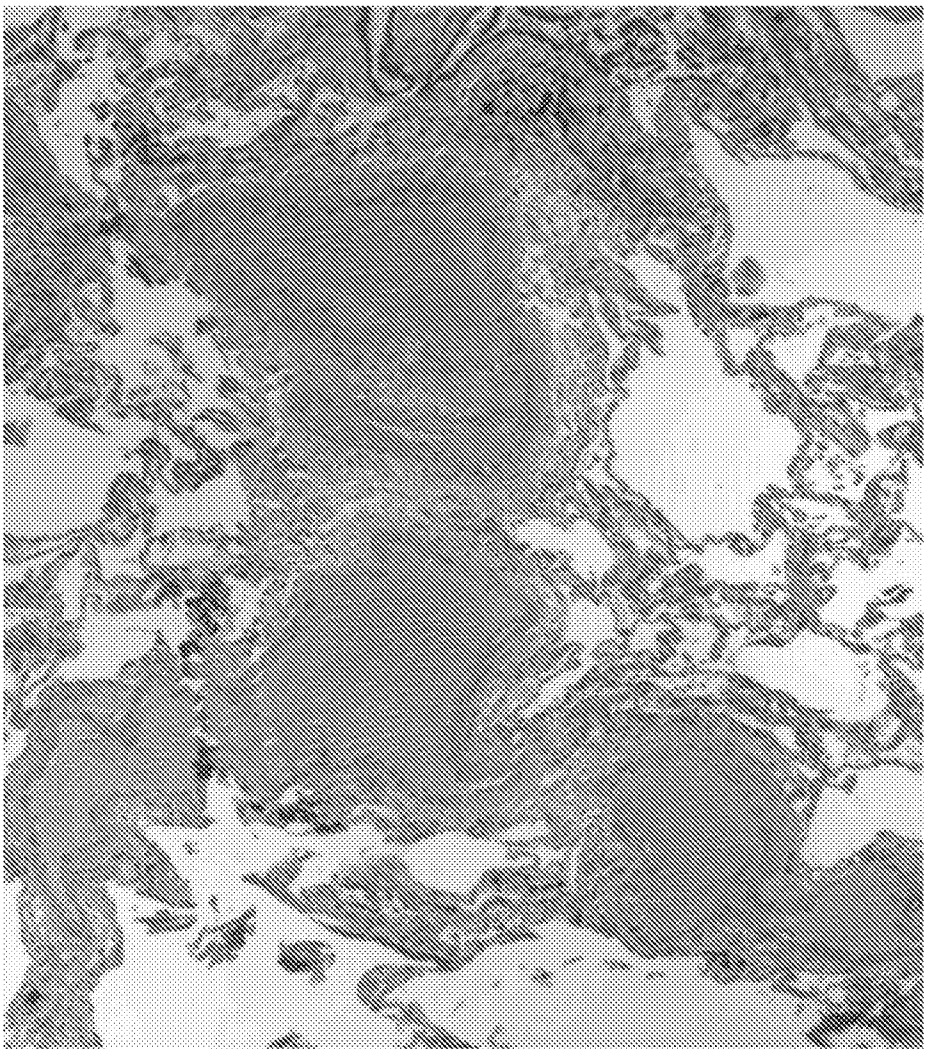


FIG. 41B

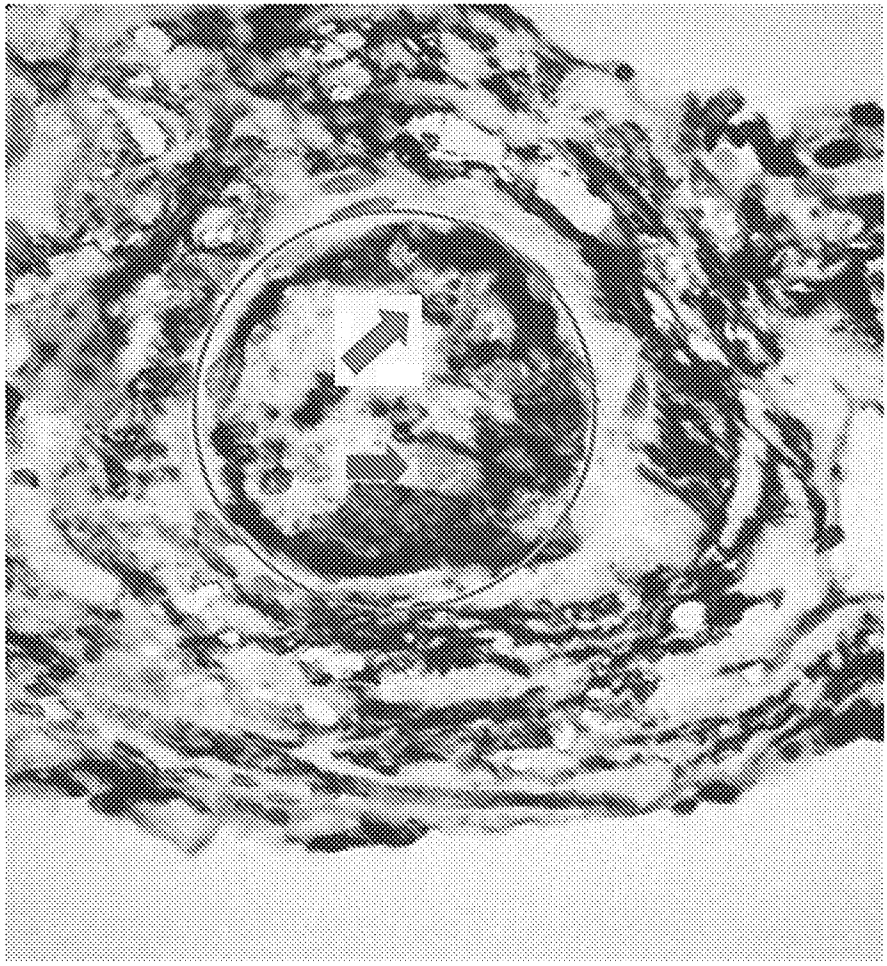


FIG. 41C



FIG. 41D

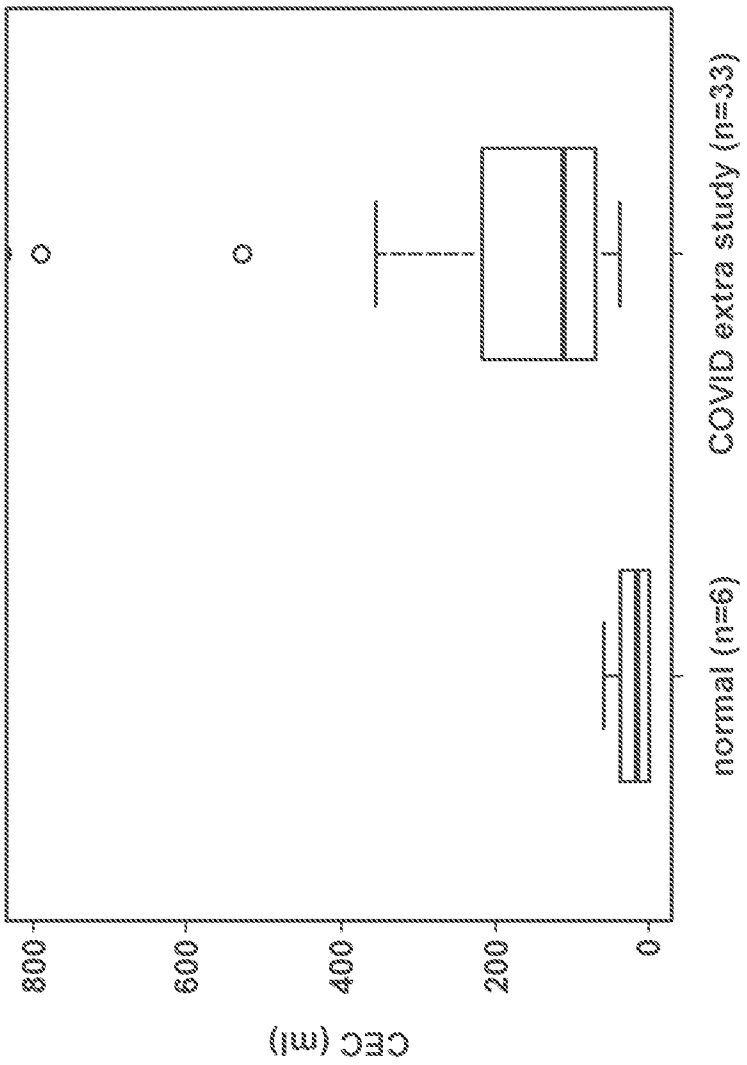


FIG. 42A

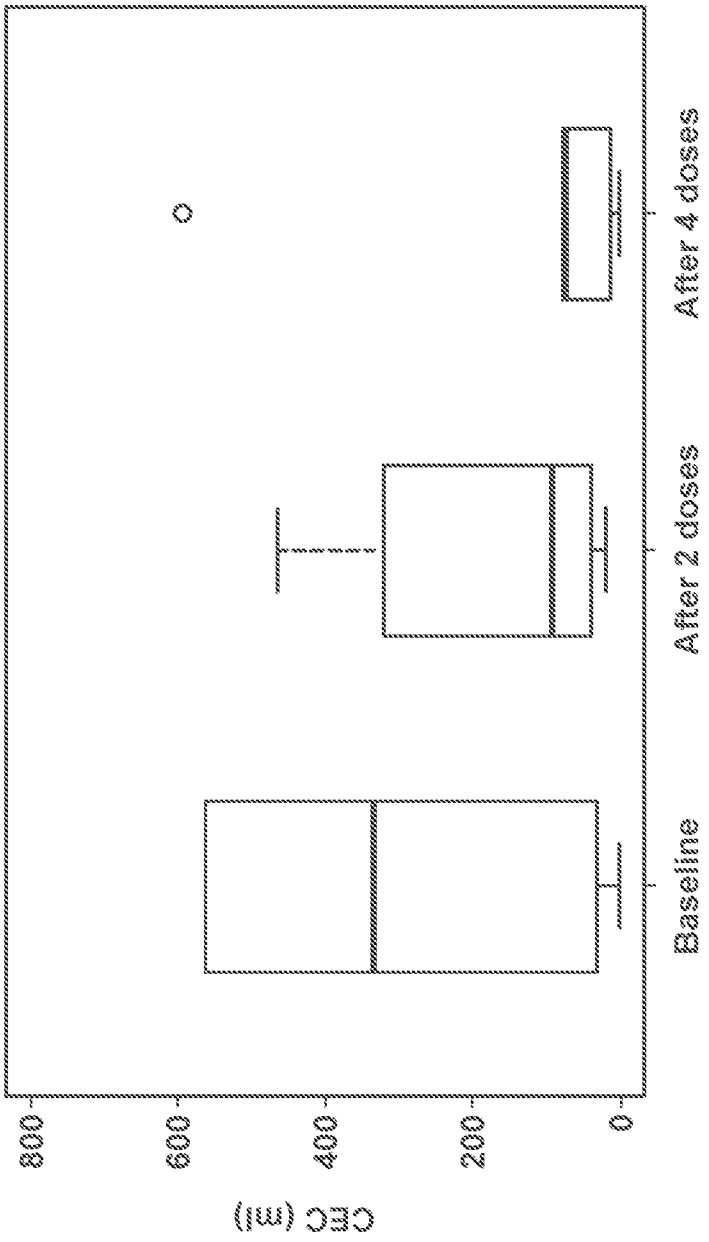


FIG. 42B

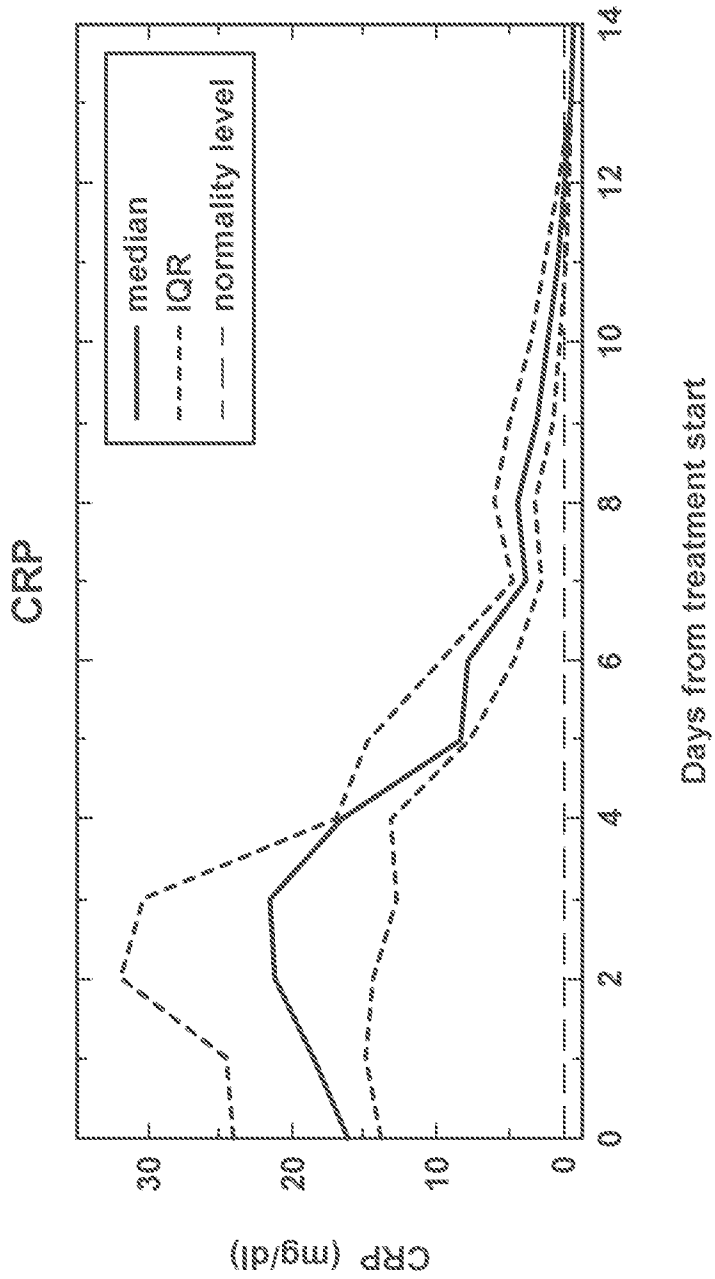

CRP
median
IQR
normality level
CRP (mg/dl)
0
10
20
30
0
2
4
6
8
10
12
14
Days from treatment start

FIG. 43

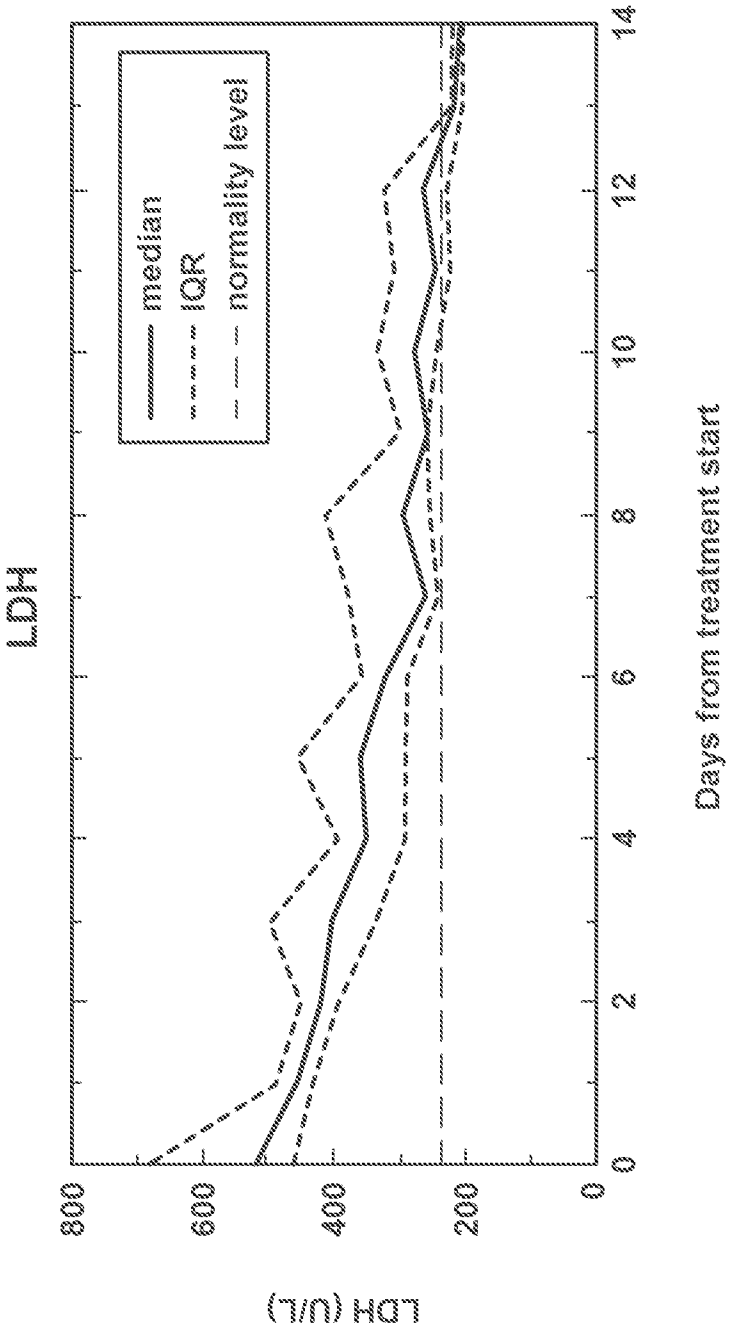

LDH
median
IQR
normality level
LDH (U/L)
800
600
400
200
0
0
2
4
6
8
10
12
14
Days from treatment start

FIG. 44

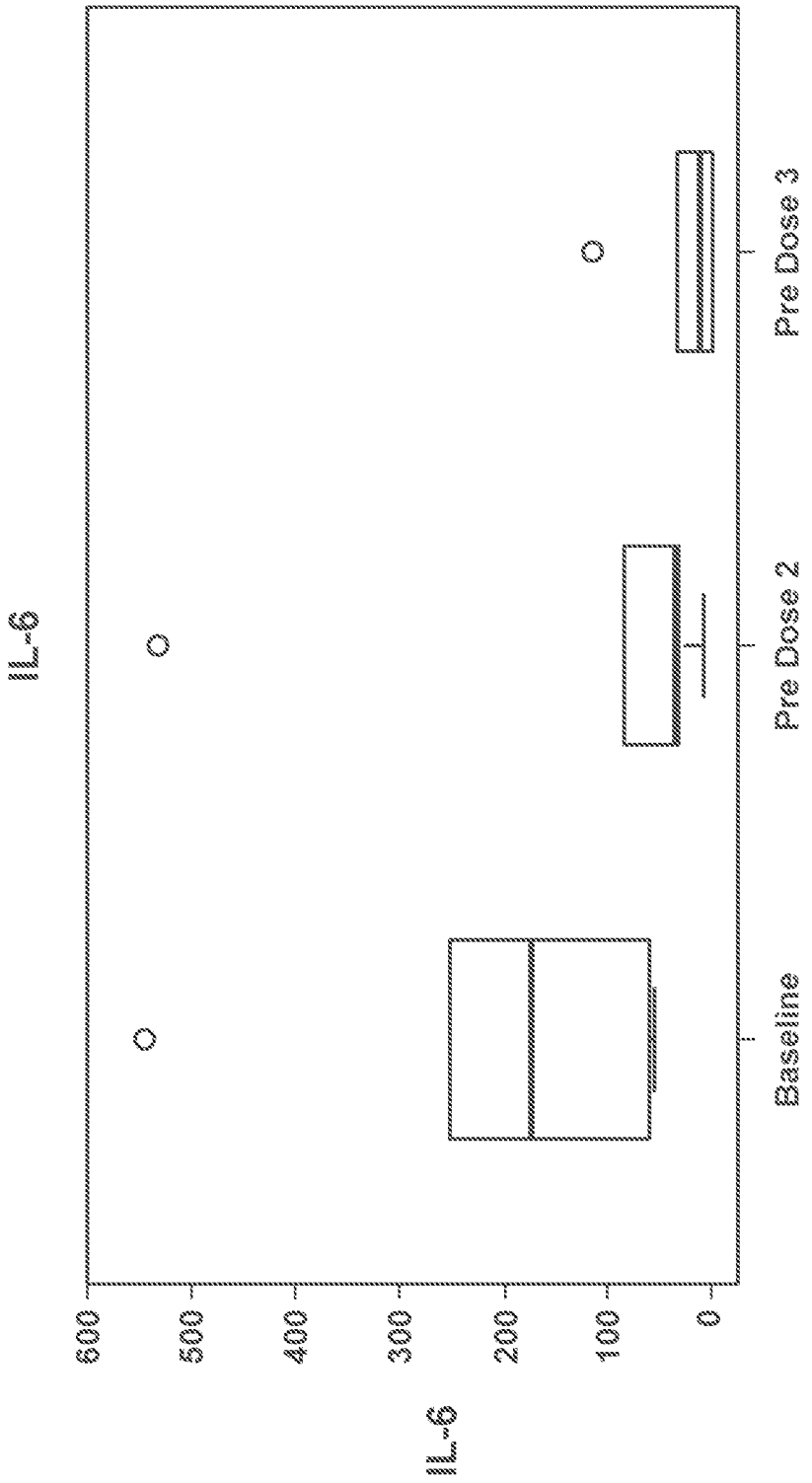


FIG. 45

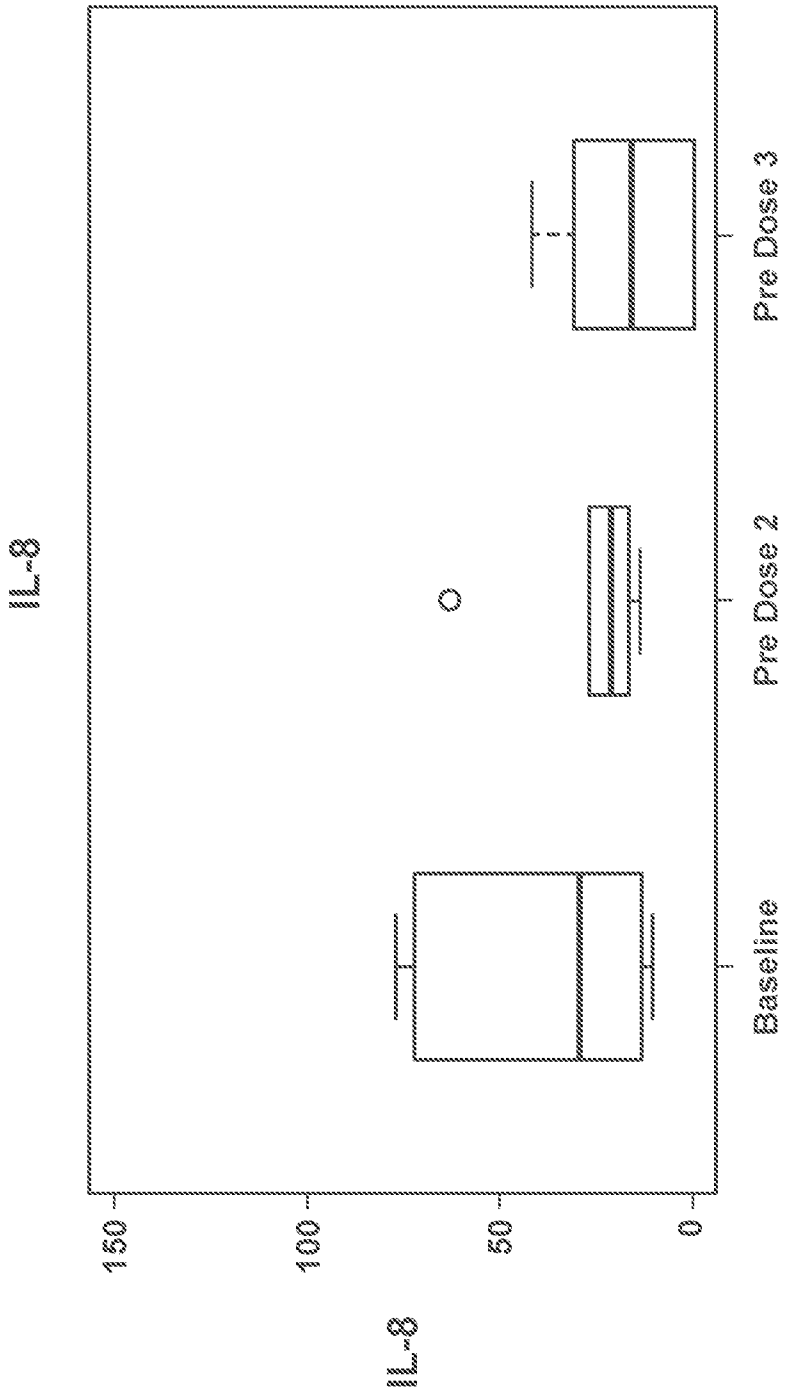


FIG. 46

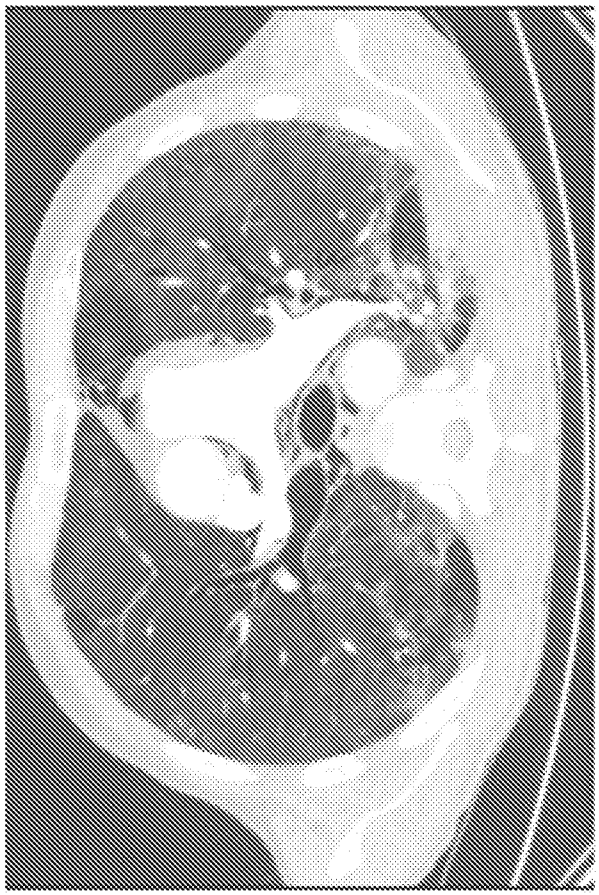


FIG. 47B



FIG. 47A

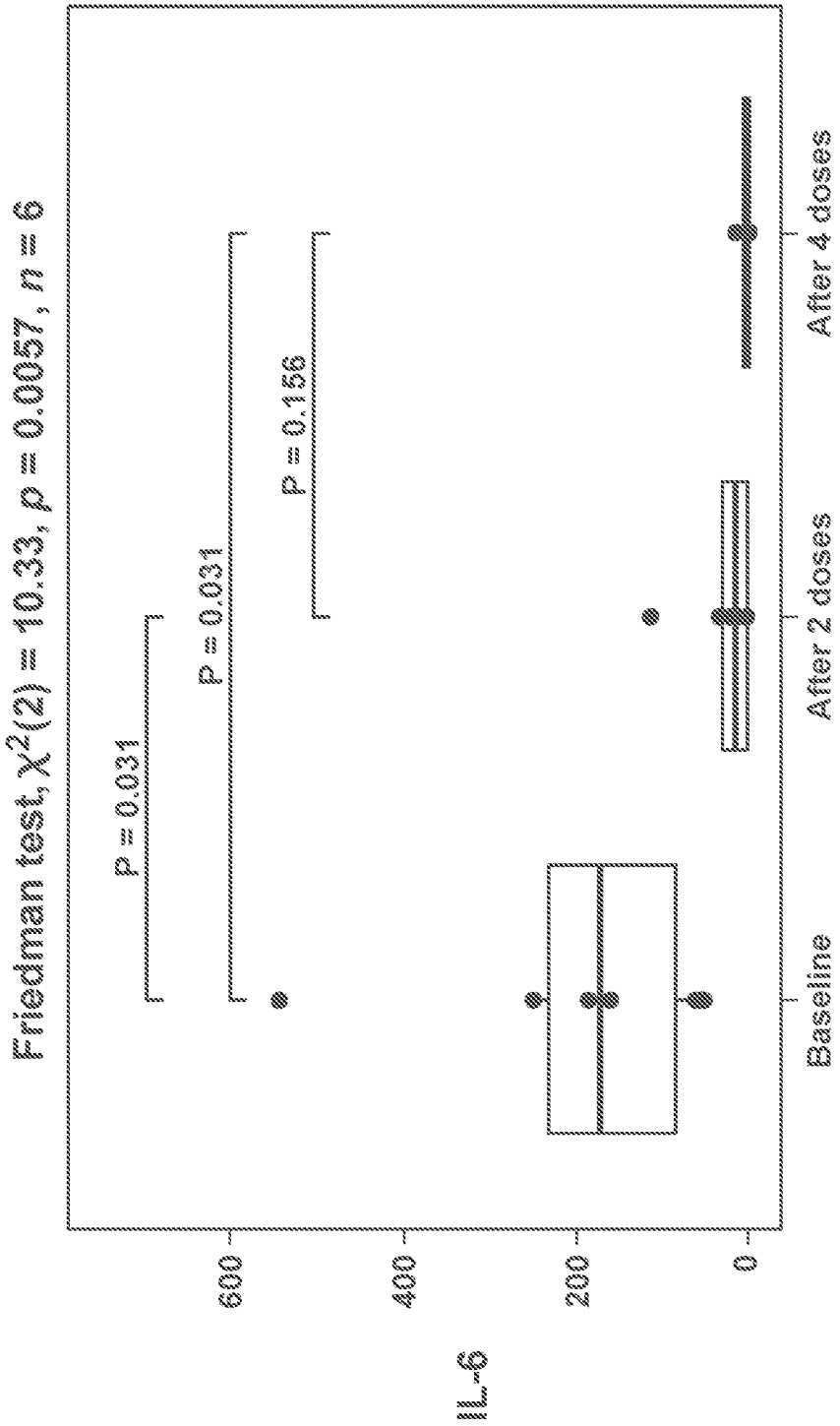

Friedman test, $\chi^2(2) = 10.33$, $p = 0.0057$, $n = 6$
P = 0.031
P = 0.031
P = 0.156
IL-6
600
400
200
0
Baseline
After 2 doses
After 4 doses

FIG. 48

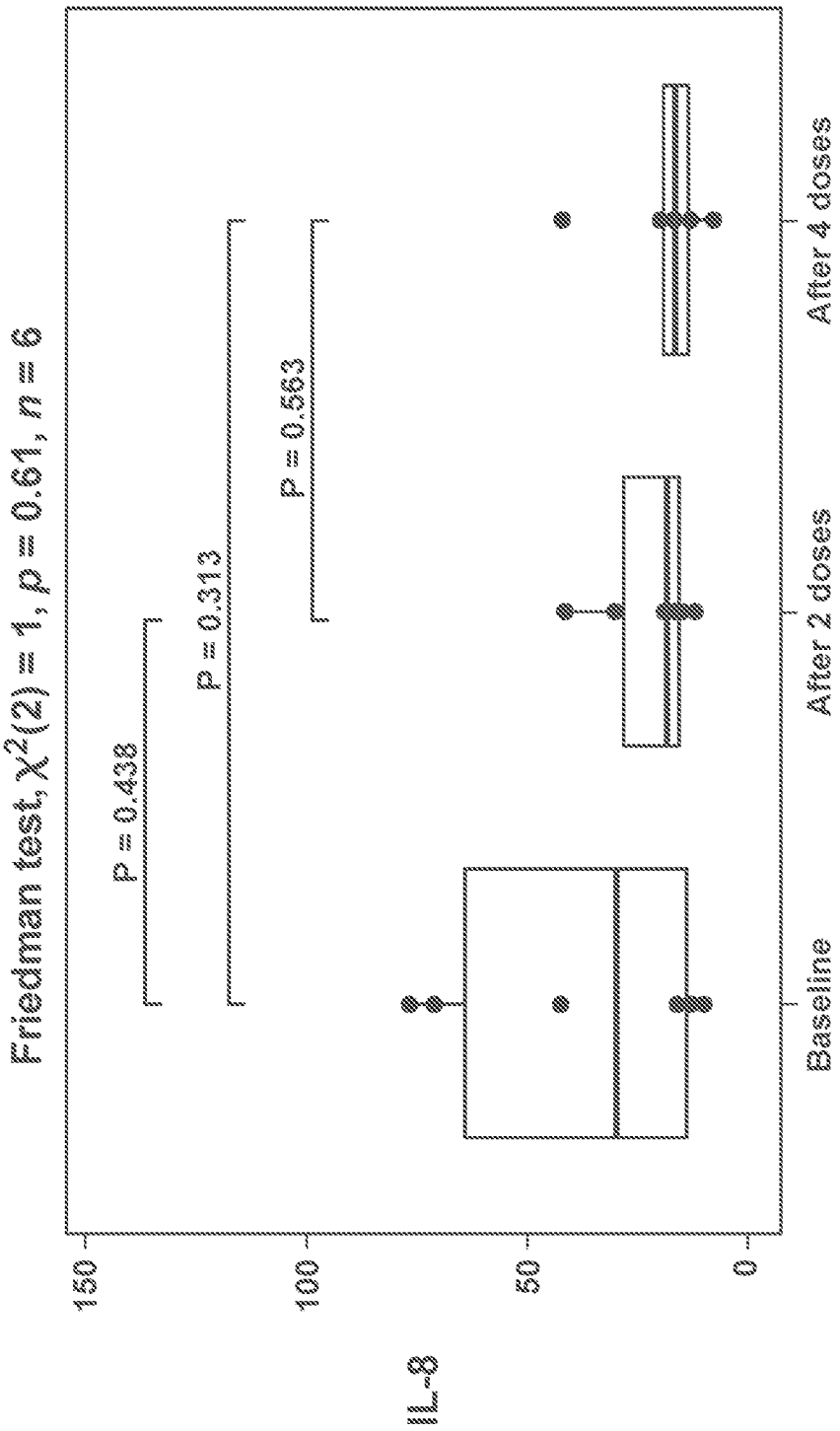

Friedman test, $\chi^2(2) = 1$, $p = 0.61$, $n = 6$
P = 0.438
P = 0.313
P = 0.563
IL-8
150
100
50
0
Baseline
After 2 doses
After 4 doses

FIG. 49

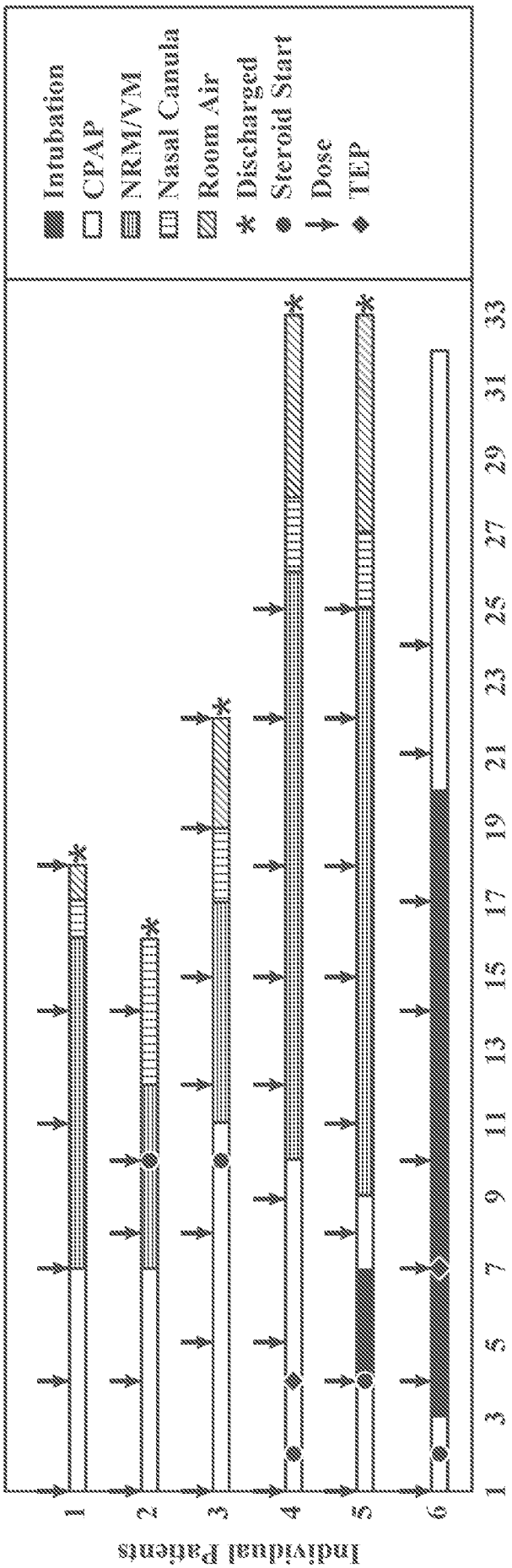

Intubation
CPAP
NRM/VM
Nasal Canula
Room Air
Discharged
Steroid Start
Dose
TEP
Individual Patients
1
2
3
4
5
6
Days from treatment start
1
3
5
7
9
11
13
15
17
19
21
23
25
27
29
31
33

FIG. 50

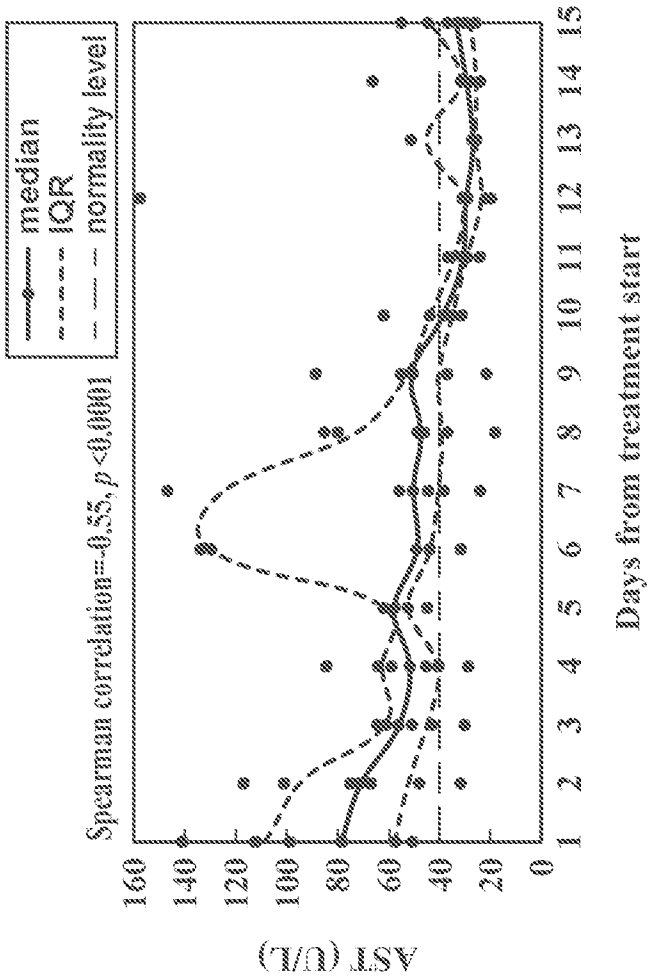

median
IQR
normality level
Spearman correlation=0,35, p <0,0001
AST (U/L)
160
140
120
100
80
60
40
20
0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Days from treatment start

FIG. 51A

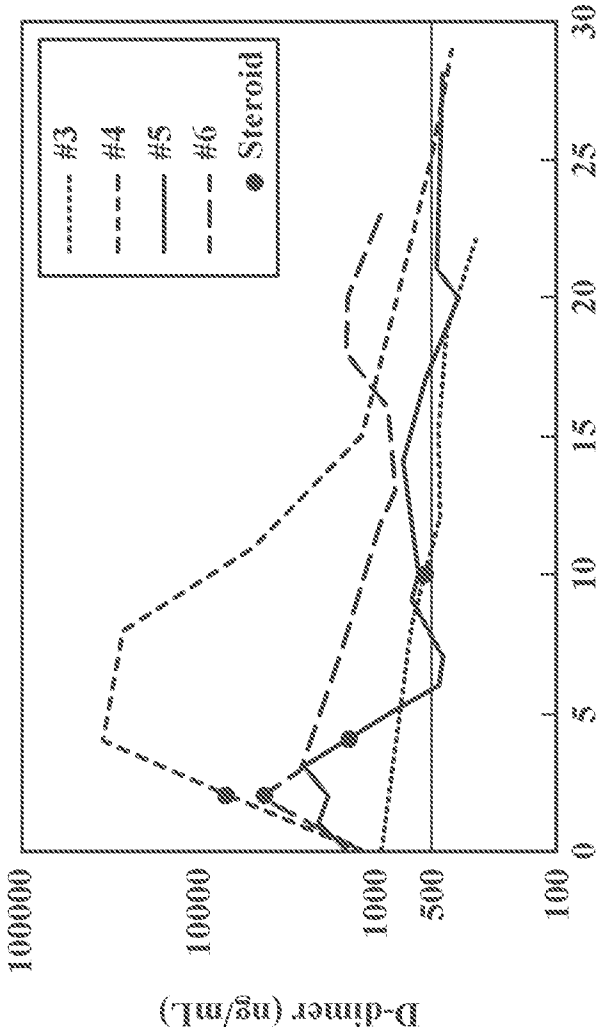

#3
#4
#5
#6
Steroid
D-dimer (ng/mL)
100000
10000
1000
500
100
0
5
10
15
20
25
30
Days from enrollment

FIG. 51B

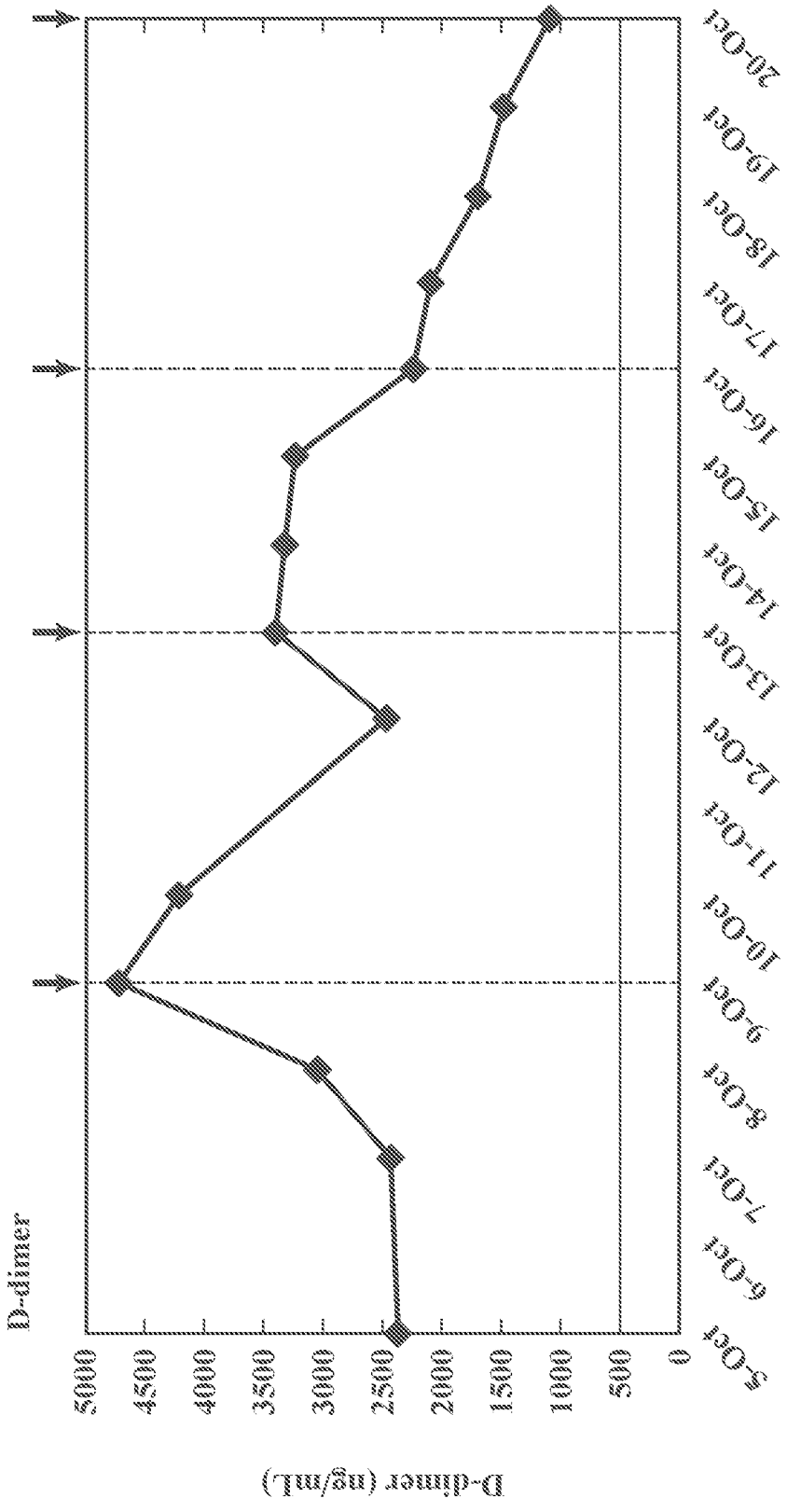

D-dimer
D-dimer (ng/mL)
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
Day-5
Day-4
Day-3
Day-2
Day-1
Day-0
Day-6
Day-8
Day-7
Day-9
Day-10
Day-11
Day-12
Day-13
Day-14
Day-15
Day-16
Day-17
Day-18
Day-19
Day-20

FIG. 52A

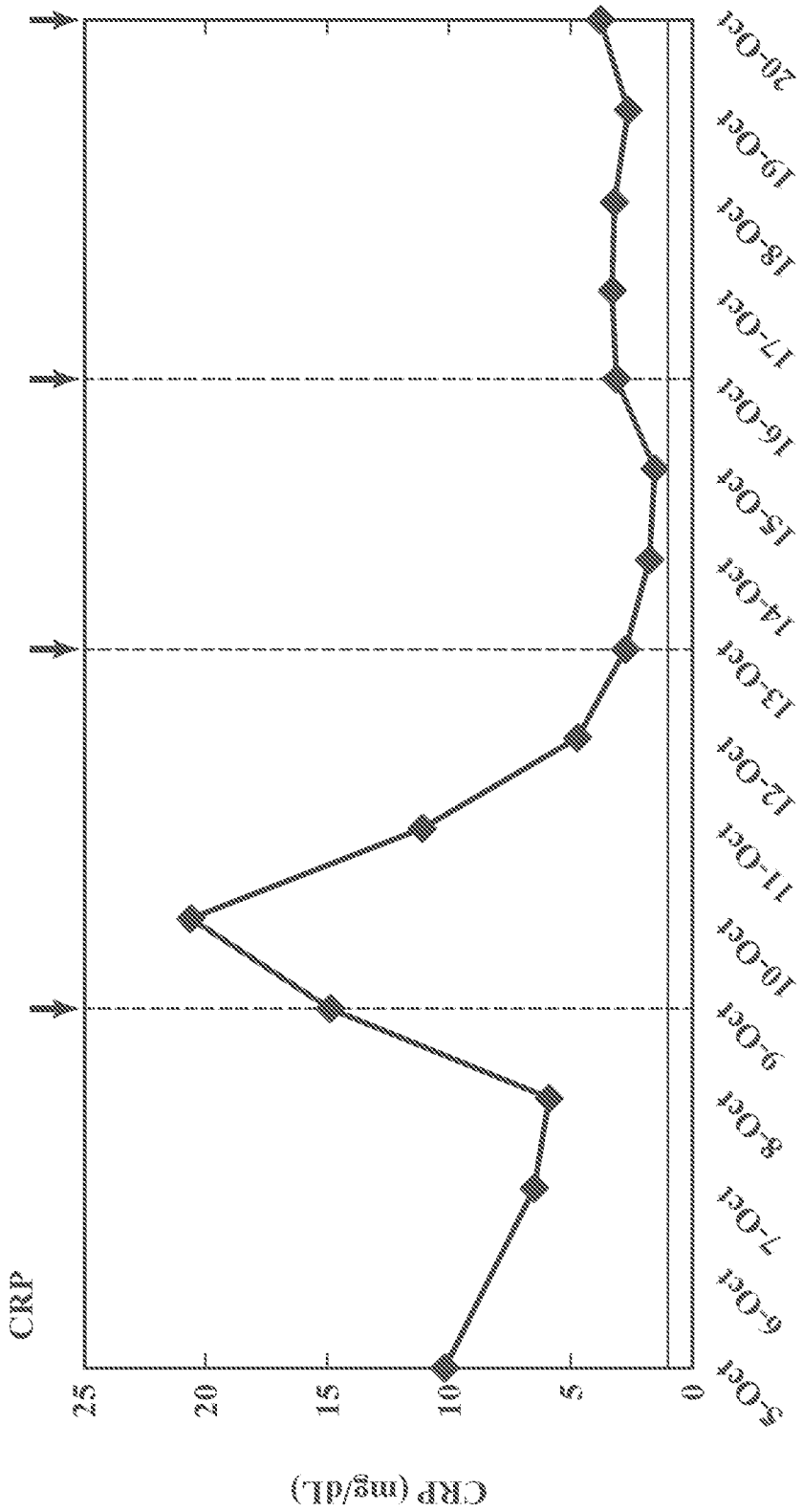

CRP
CRP (mg/dL)
25
20
15
10
5
0
S00-
900-
700-
800-
600-
100-
110-
120-
130-
140-
150-
160-
170-
180-
190-
200-

FIG. 52B

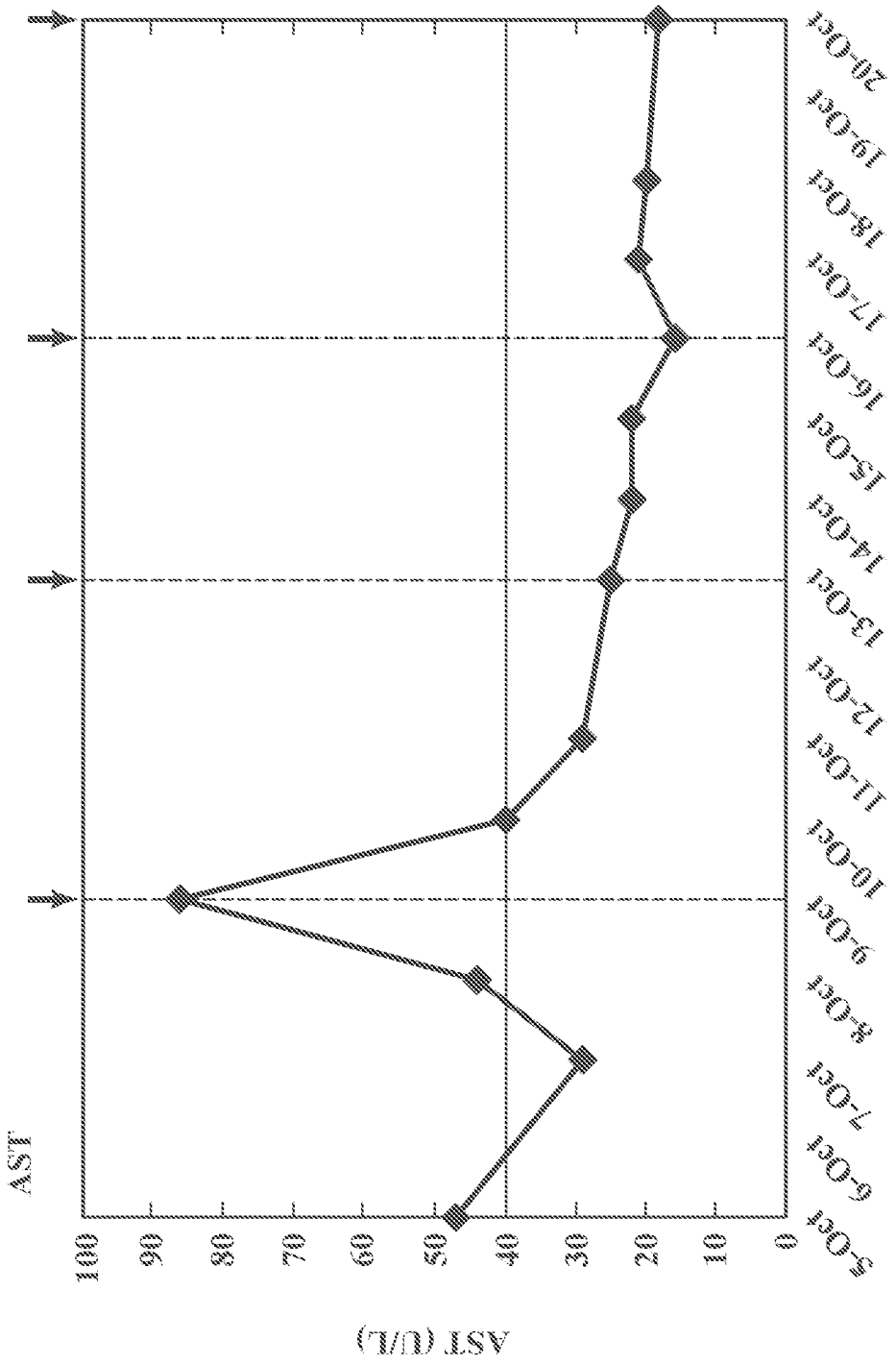

AST
AST (U/L)
100
90
80
70
60
50
40
30
20
10
0
5-Oct
6-Oct
7-Oct
8-Oct
9-Oct
10-Oct
11-Oct
12-Oct
13-Oct
14-Oct
15-Oct
16-Oct
17-Oct
18-Oct
19-Oct
20-Oct

FIG. 52C

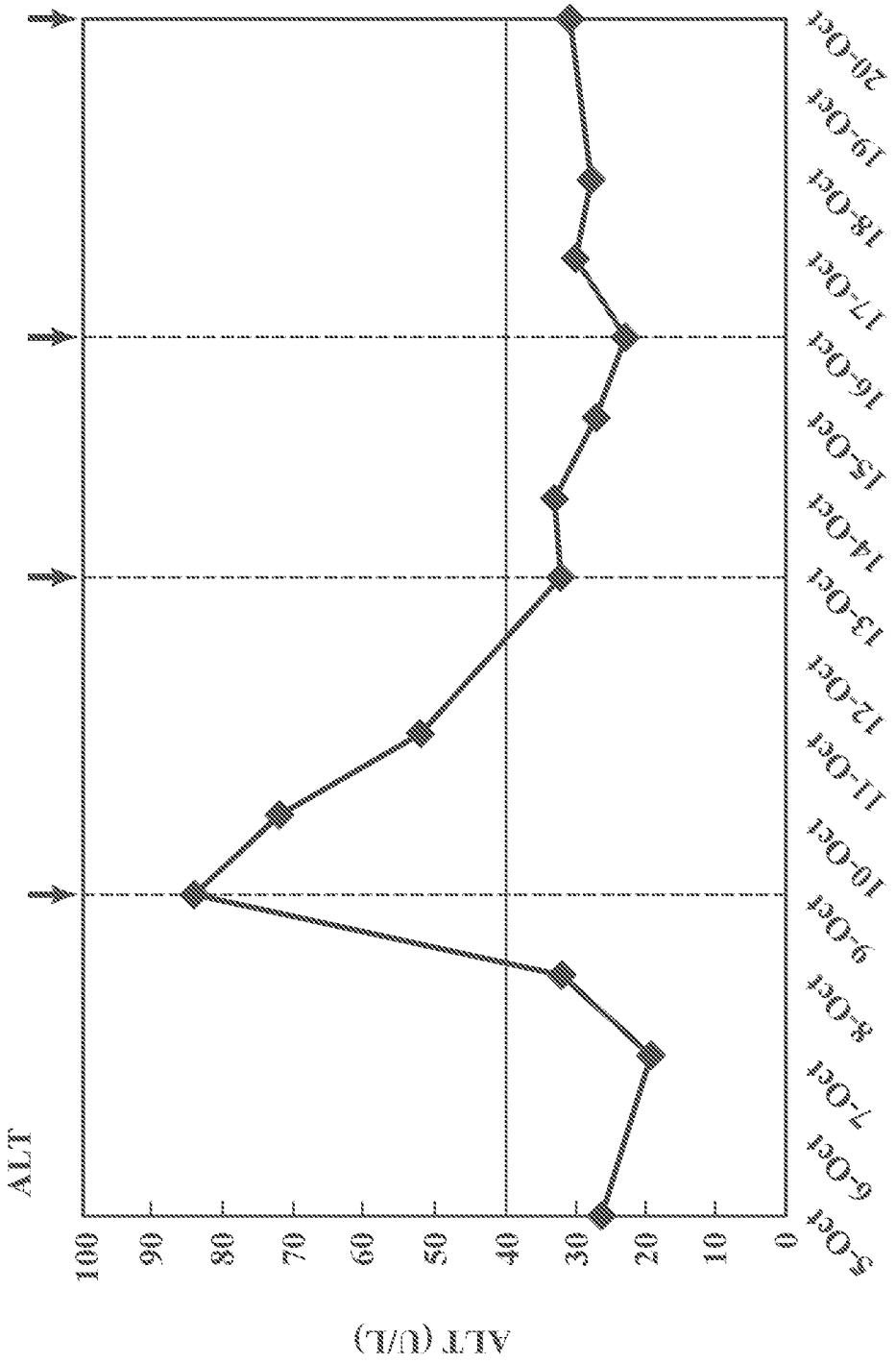

ALT
ALT (U/L)
100
90
80
70
60
50
40
30
20
10
0
5-Oct
6-Oct
7-Oct
8-Oct
9-Oct
10-Oct
11-Oct
12-Oct
13-Oct
14-Oct
15-Oct
16-Oct
17-Oct
18-Oct
19-Oct
20-Oct

FIG. 52D

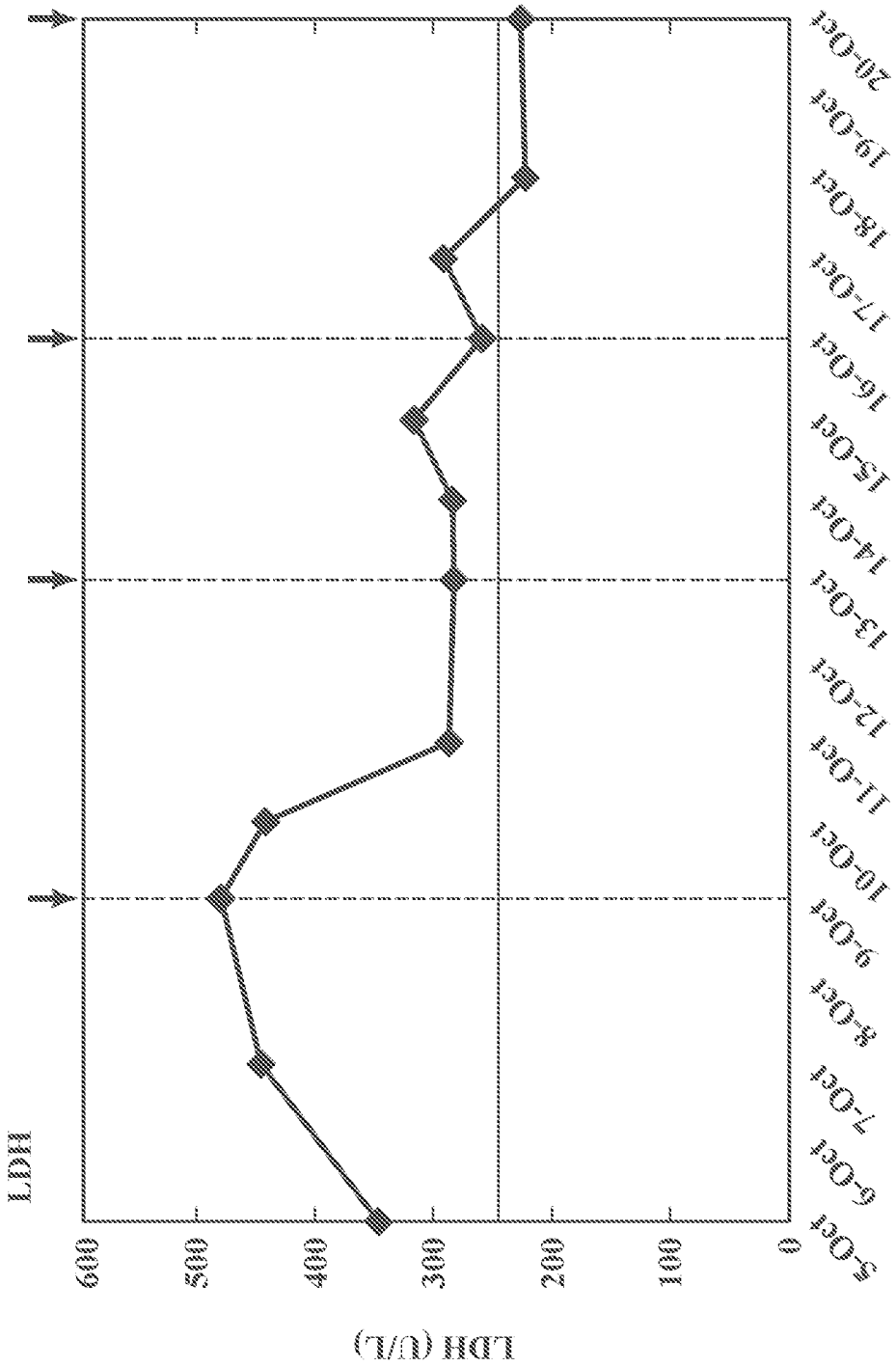

LDH
LDH (U/L)
600
500
400
300
200
100
0
5-Oct
6-Oct
7-Oct
8-Oct
9-Oct
10-Oct
11-Oct
12-Oct
13-Oct
14-Oct
15-Oct
16-Oct
17-Oct
18-Oct
19-Oct
20-Oct

FIG. 52E

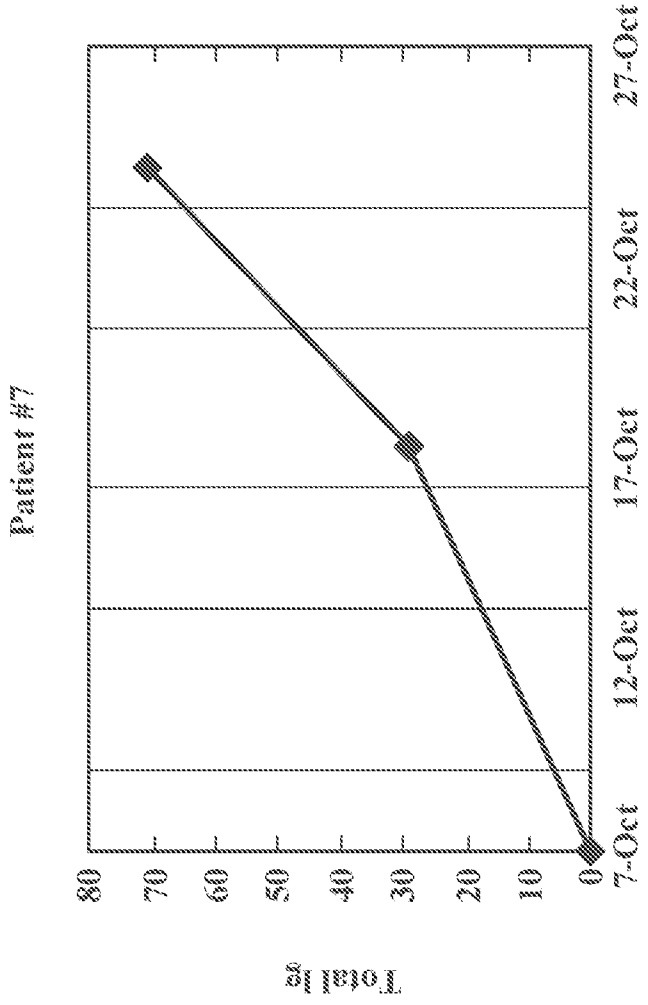

Patient #7
Total lbs
80
70
60
50
40
30
20
10
0
7-Oct
12-Oct
17-Oct
22-Oct
27-Oct

FIG. 53

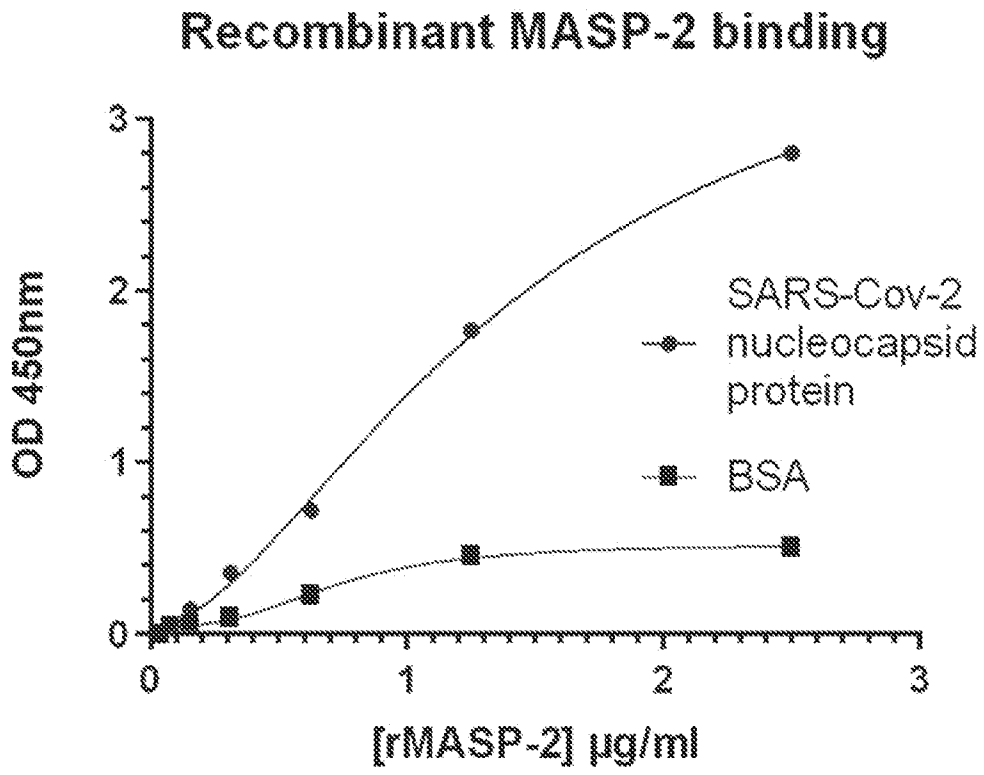

Recombinant MASP-2 binding
OD 450nm
0
1
2
3
0
1
2
3
[rMASP-2] µg/ml
SARS-Cov-2 nucleocapsid protein
BSA

FIG. 54

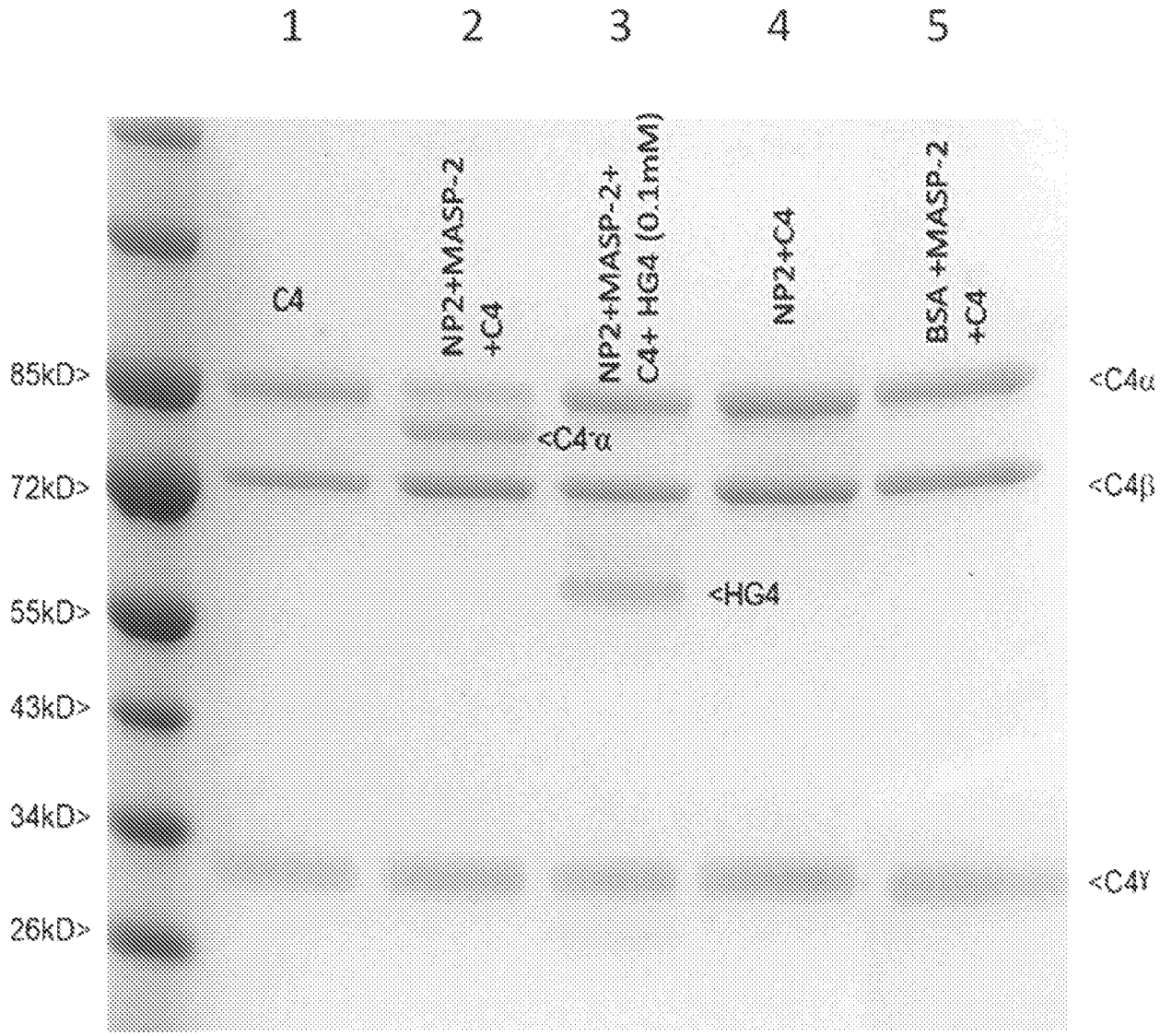

1
2
3
4
5
C4
NP2+MASP-2 +C4
NP2+MASP-2+ C4+ HG4 (0.1mM)
NP2+C4
BSA +MASP-2 +C4
85kD>
72kD>
55kD>
43kD>
34kD>
26kD>
<C4α
<C4α
<C4β
<HG4
<C4γ

FIG. 55

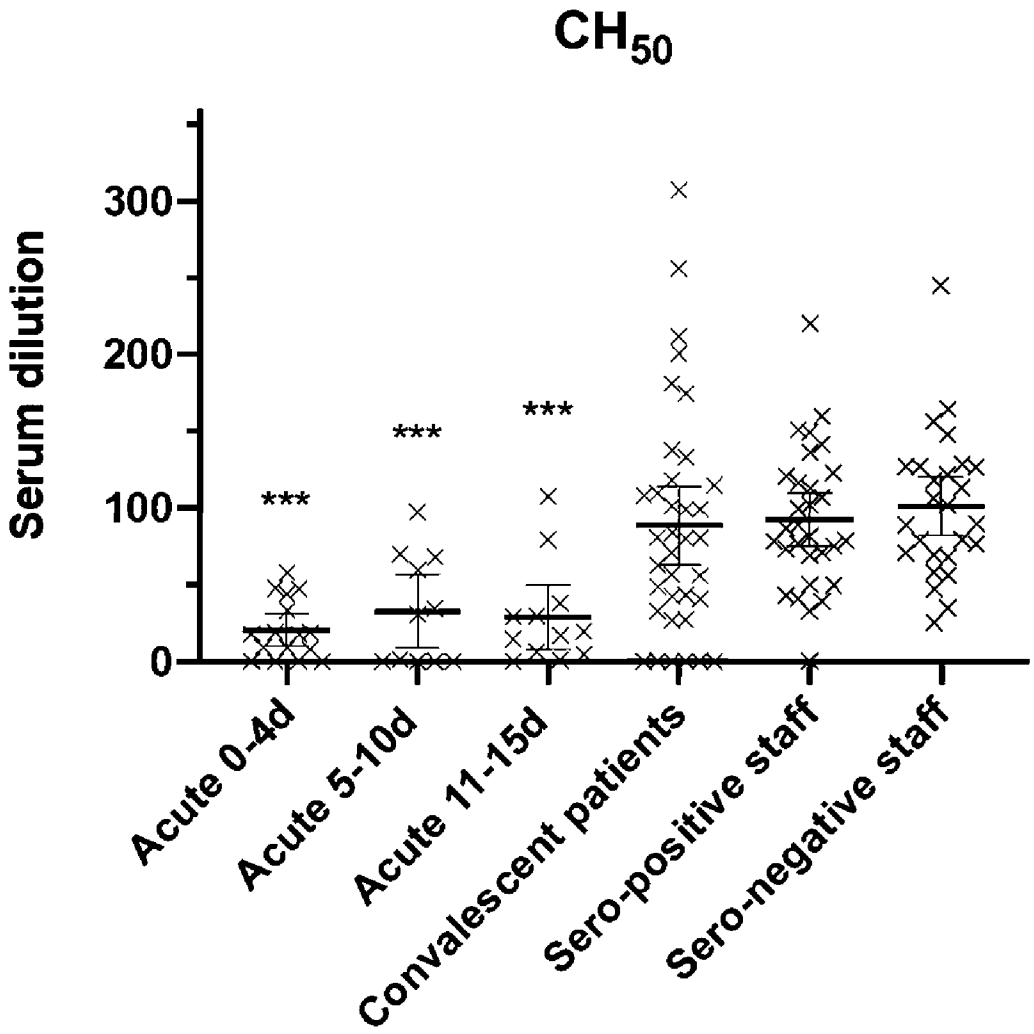

CH50
Serum dilution
300
200
100
0
***
***
***
Acute 0-4d
Acute 5-10d
Acute 11-15d
Convalescent patients
Sero-positive staff
Sero-negative staff

FIG. 56

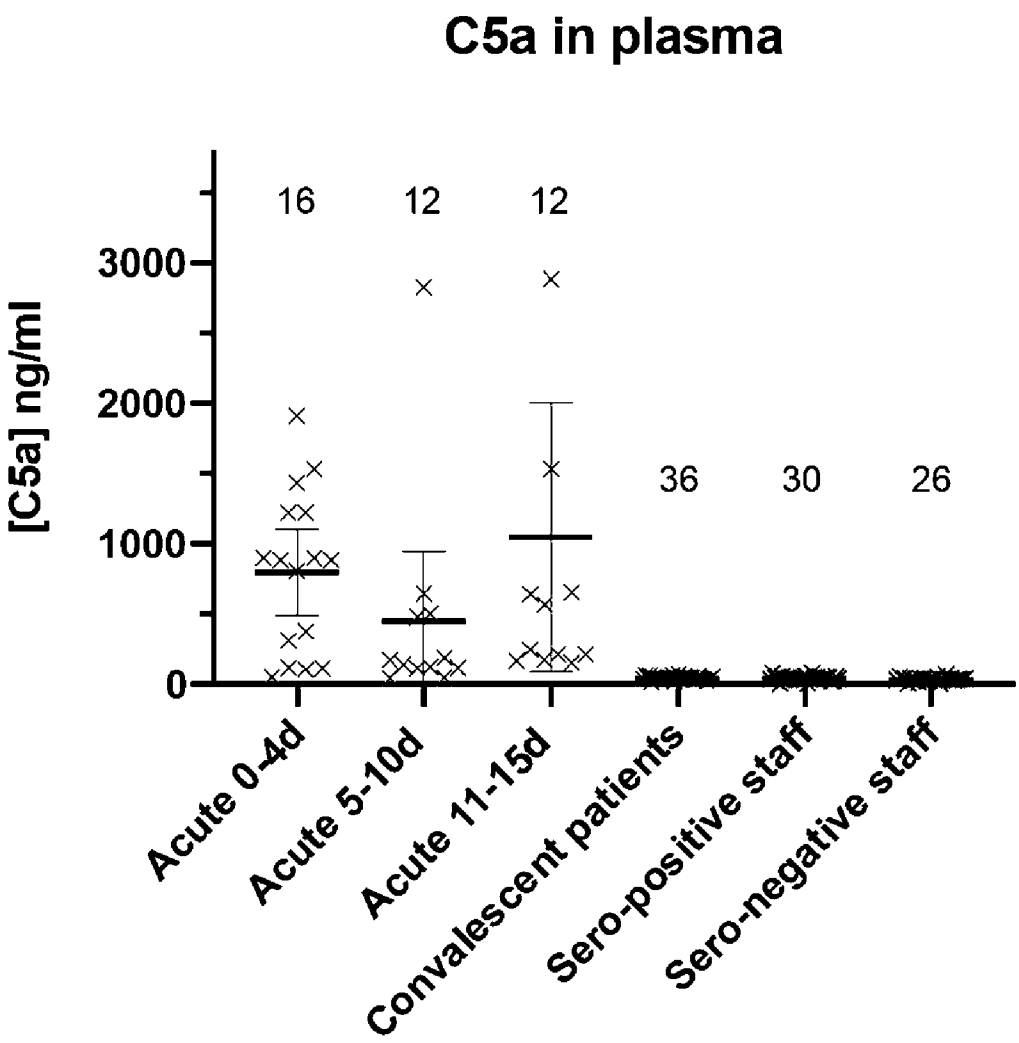

C5a in plasma
[C5a] ng/ml
3000
2000
1000
0
16
12
12
36
30
26
Acute 0-4d
Acute 5-10d
Acute 11-15d
Convalescent patients
Sero-positive staff
Sero-negative staff

FIG. 57

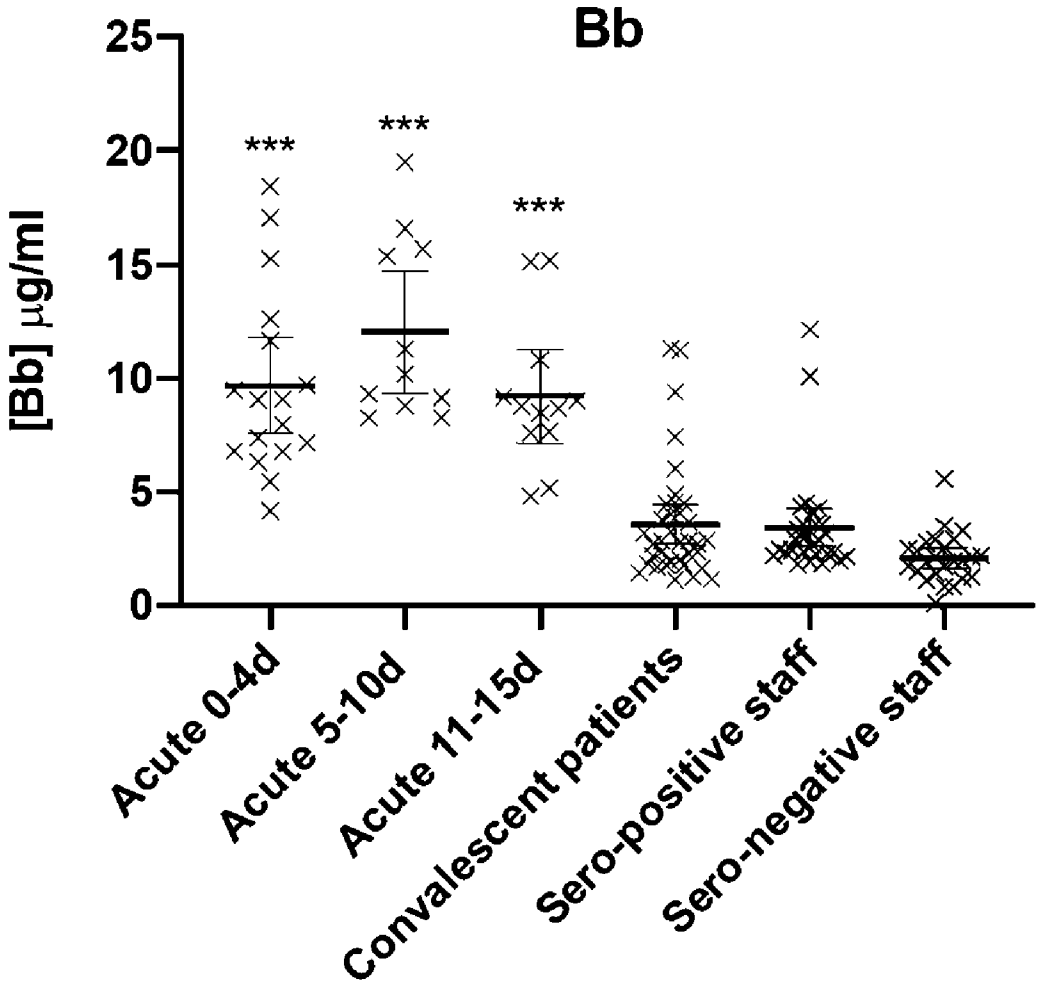

Bb
[Bb] µg/ml
25
20
15
10
5
0
***
***
***
Acute 0-4d
Acute 5-10d
Acute 11-15d
Convalescent patients
Sero-positive staff
Sero-negative staff

FIG. 58

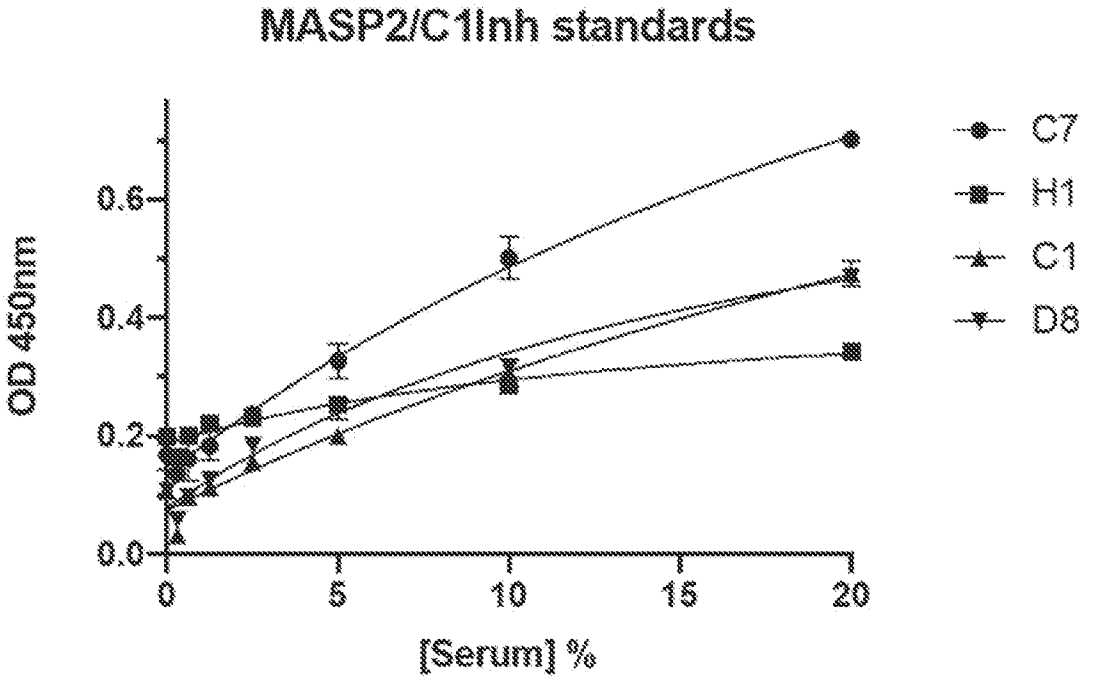

MASP2/C1Inh standards
OD 450nm
0.0
0.2
0.4
0.6
0
5
10
15
20
[Serum] %
C7
H1
C1
D8

FIG. 59

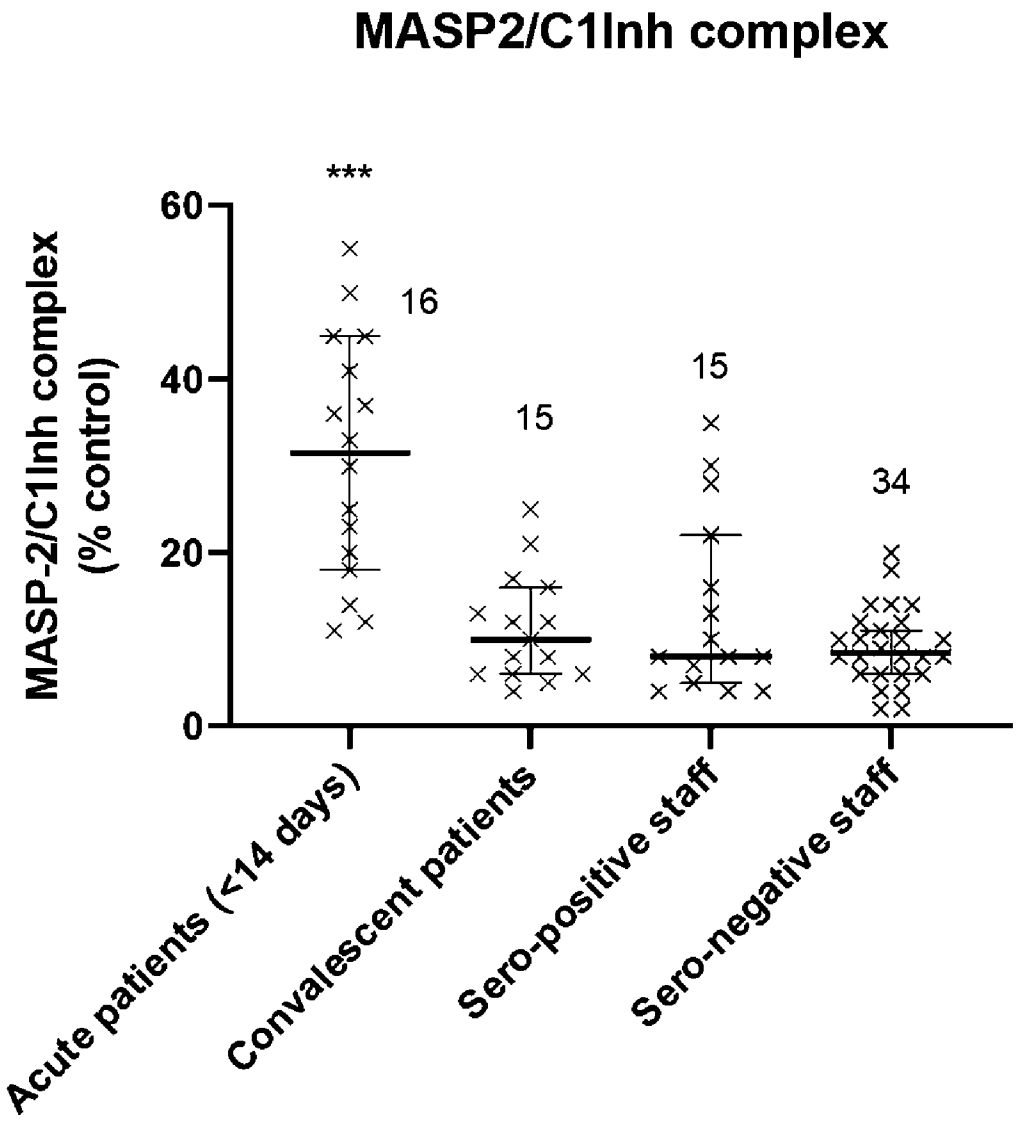

MASP2/C1Inh complex
MASP-2/C1Inh complex (% control)
60
40
20
0
***
16
15
15
34
Acute patients (<14 days)
Convalescent patients
Sero-positive staff
Sero-negative staff

FIG. 60

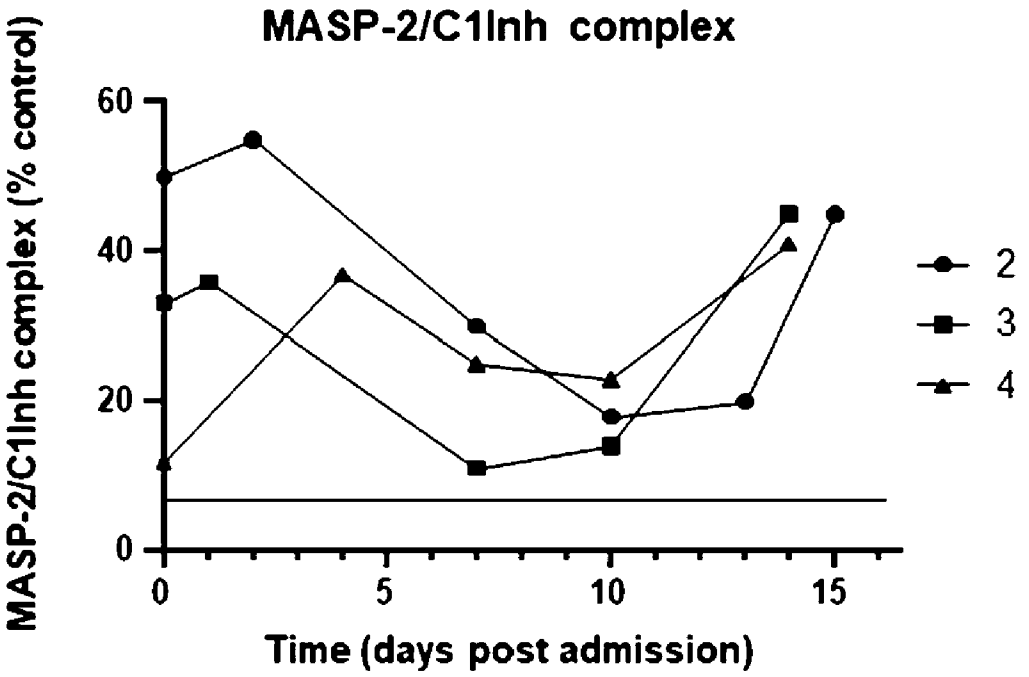

MASP-2/C1Inh complex
MASP-2/C1Inh complex (% control)
60
40
20
0
0
5
10
15
Time (days post admission)
2
3
4

FIG. 61

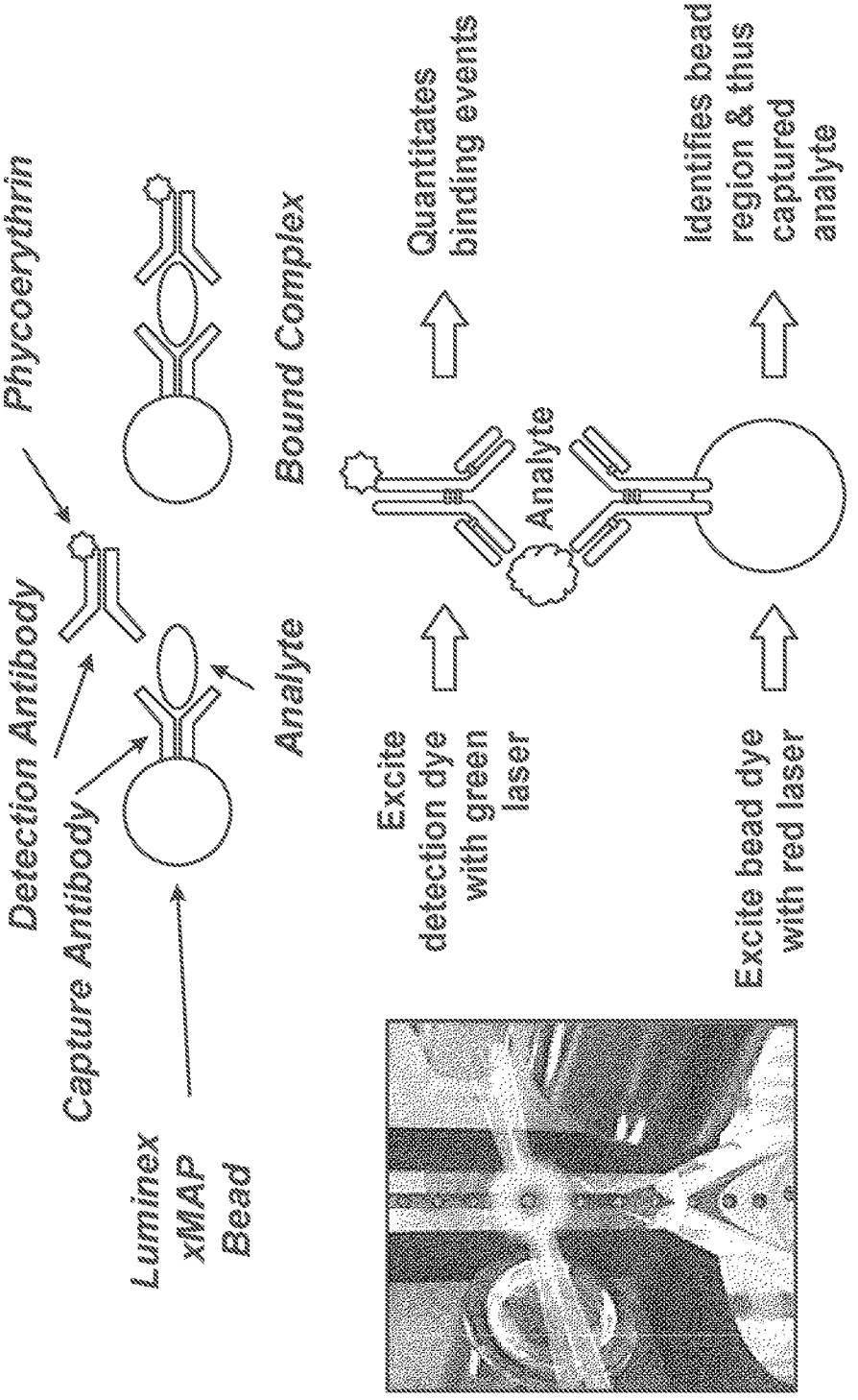

Luminex xMAP Bead
Capture Antibody
Detection Antibody
Phycoerythrin
Analyte
Bound Complex
Excite detection dye with green laser
Analyte
Quantitates binding events
Excite bead dye with red laser
Identifies bead region & thus captured analyte

FIG. 62

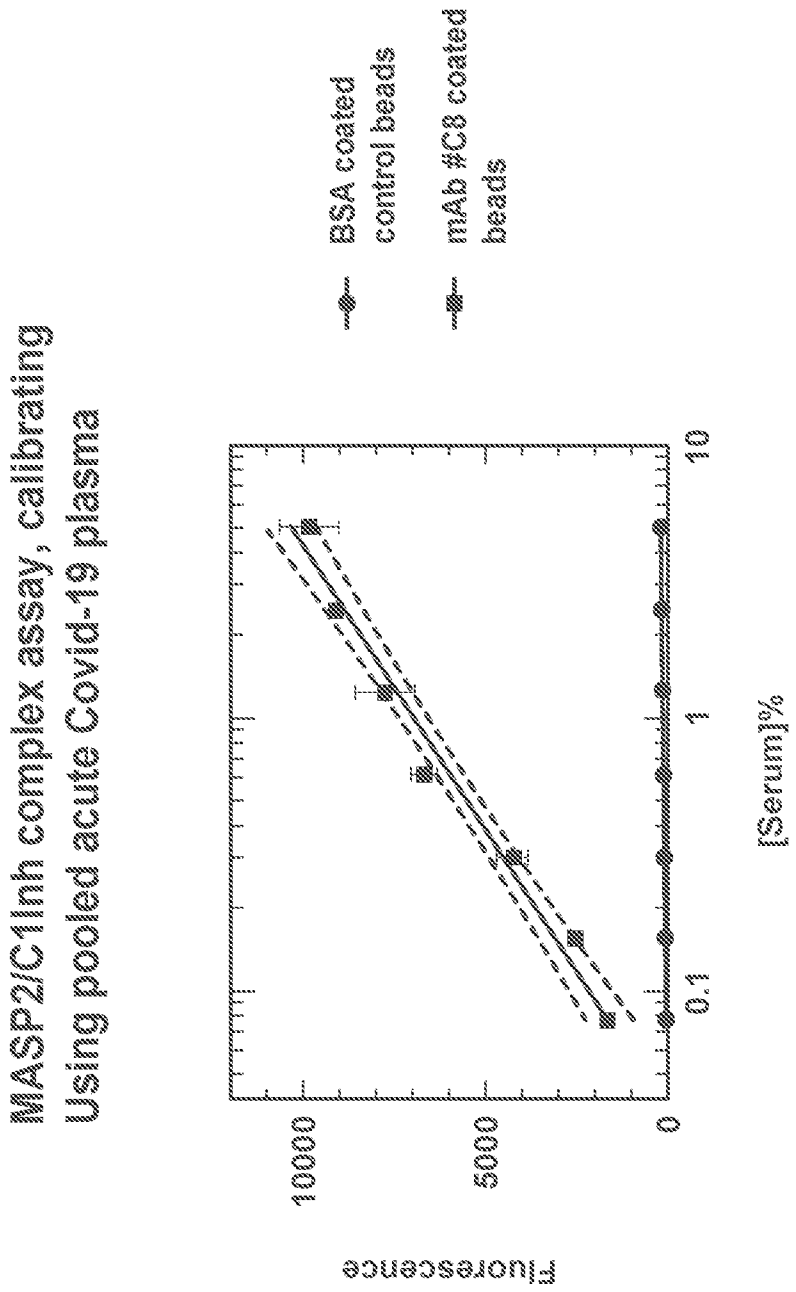

MASP2/C1Inh complex assay, calibrating
Using pooled acute Covid-19 plasma
BSA coated
control beads
mAb #C8 coated
beads
Fluorescence
10000
5000
0
0.1
1
10
[Serum]%

FIG. 63

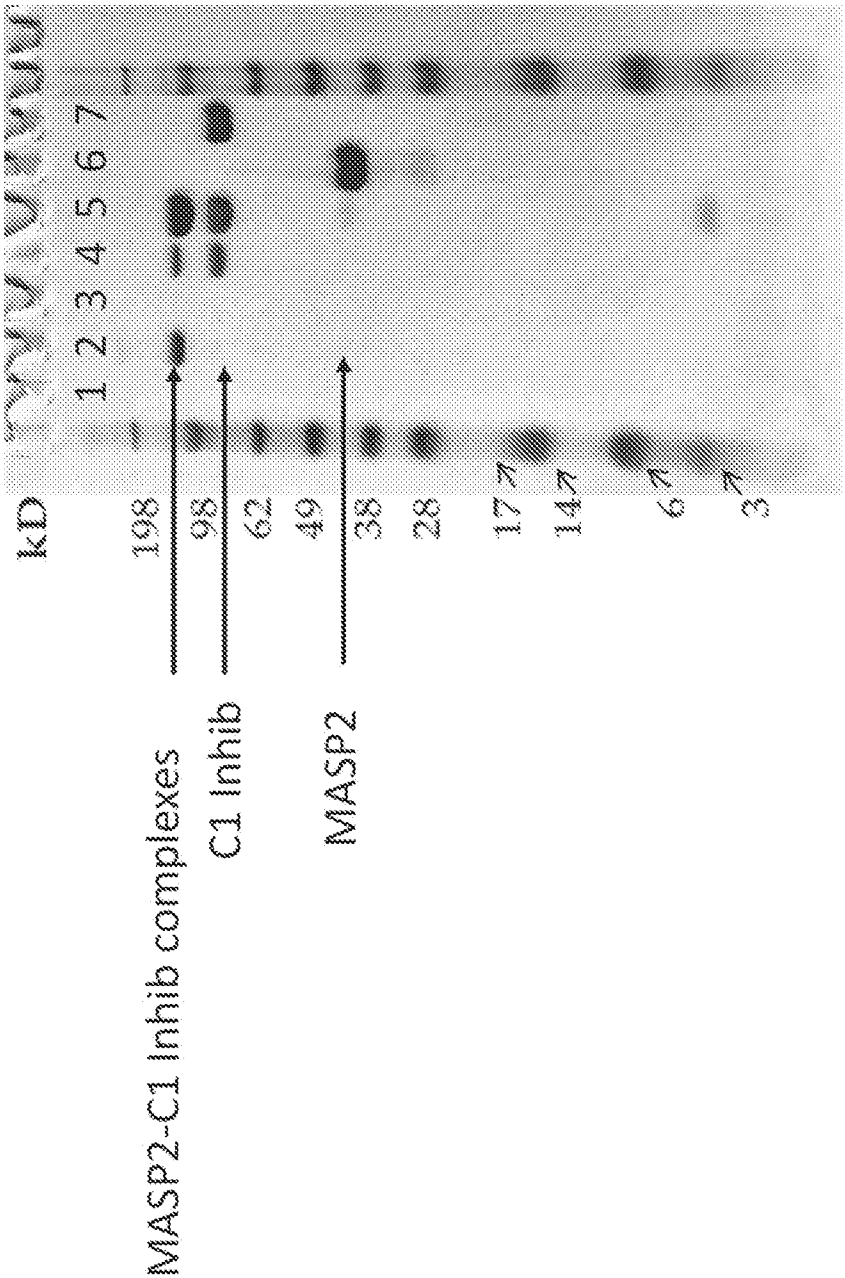

kD
1 2 3 4 5 6 7
198
98
62
49
38
28
17
14
6
3
MASP2-C1 Inhib complexes
C1 Inhib
MASP2

FIG. 64

MASP-2/C1Inh complex
<0.0001
0.0002
<0.0001
BSA control
0-4 days
5-10 days
Day 11 - discharge
3m follow-up
Seropositive HCW
Healthy controls
0
500
1000
Fluorescence

FIG. 65

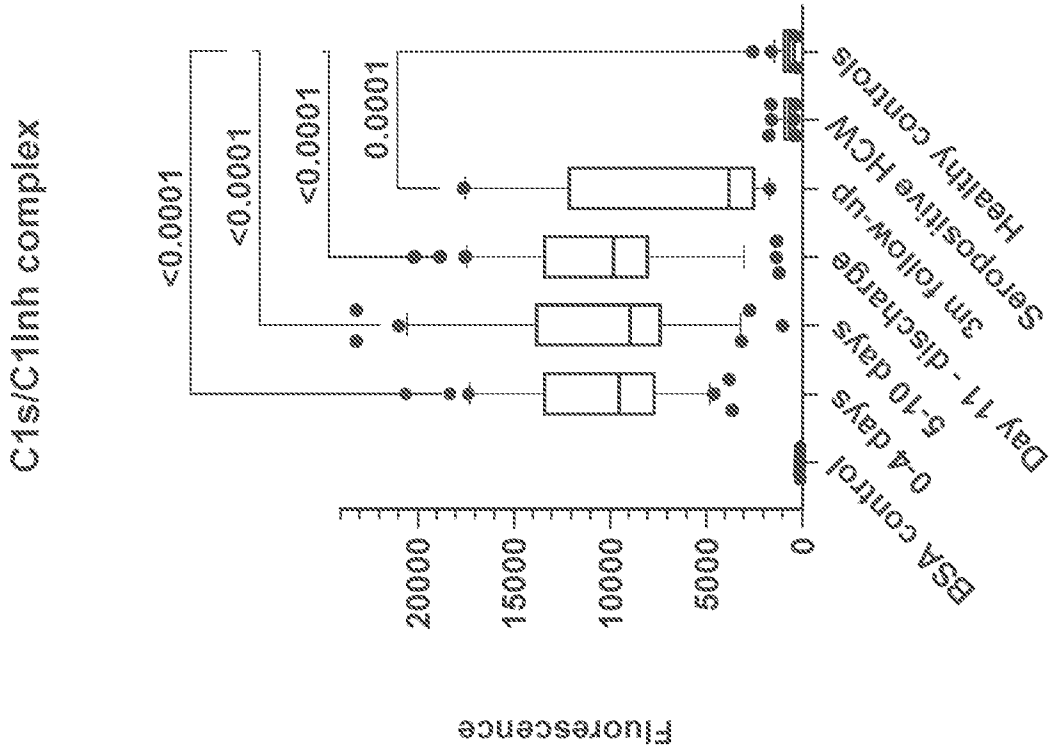

C1s/C1inh complex
<0.0001
<0.0001
<0.0001
0.0001
Fluorescence
20000
15000
10000
5000
0
BSA control
0-4 days
5-10 days
Day 11 - discharge
3m follow-up
Seropositive HCW
Healthy controls

FIG. 66

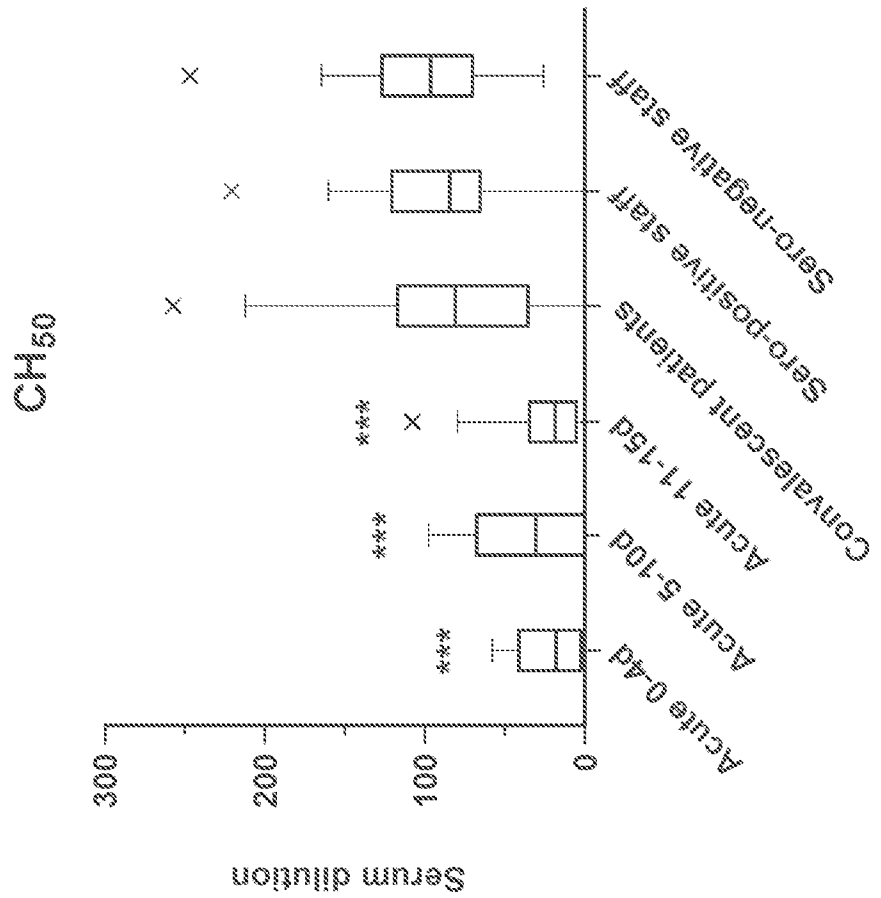

CH50
Serum dilution
300
200
100
0
Acute 0-4d
Acute 5-10d
Acute 11-15d
Convalescent patients
Sero-positive staff
Sero-negative staff
***
***
***

FIG. 67

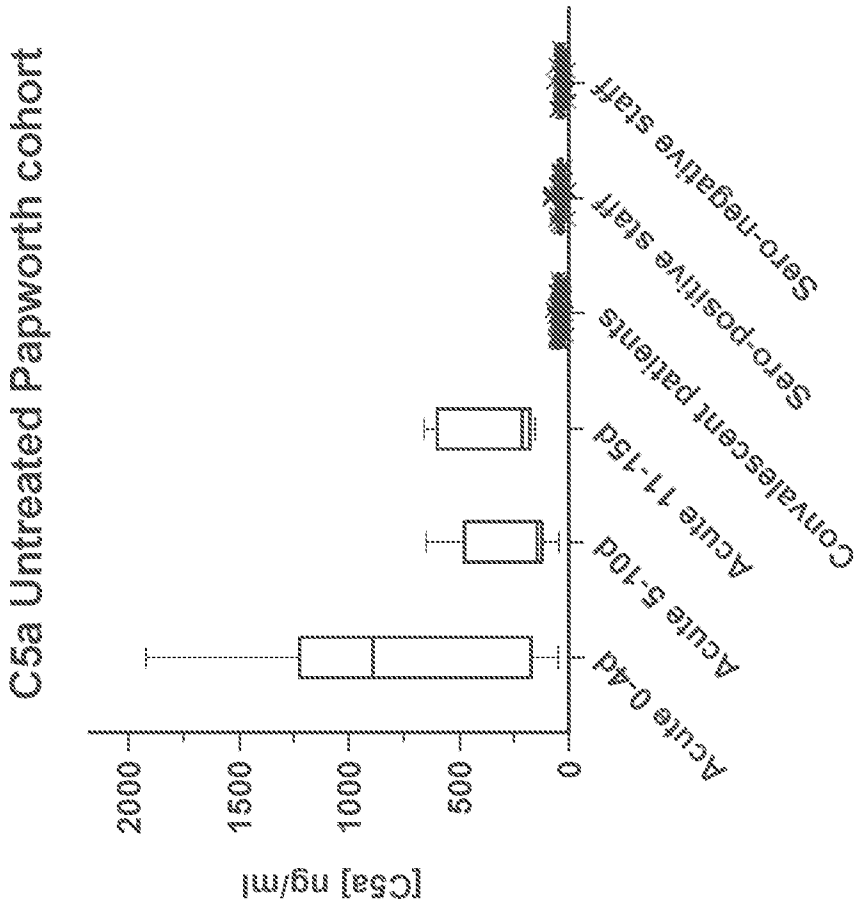

C5a Untreated Papworth cohort
[C5a] ng/ml
2000
1500
1000
500
0
Acute 0-4d
Acute 5-10d
Acute 11-15d
Convalescent patients
Sero-positive staff
Sero-negative staff

FIG. 68

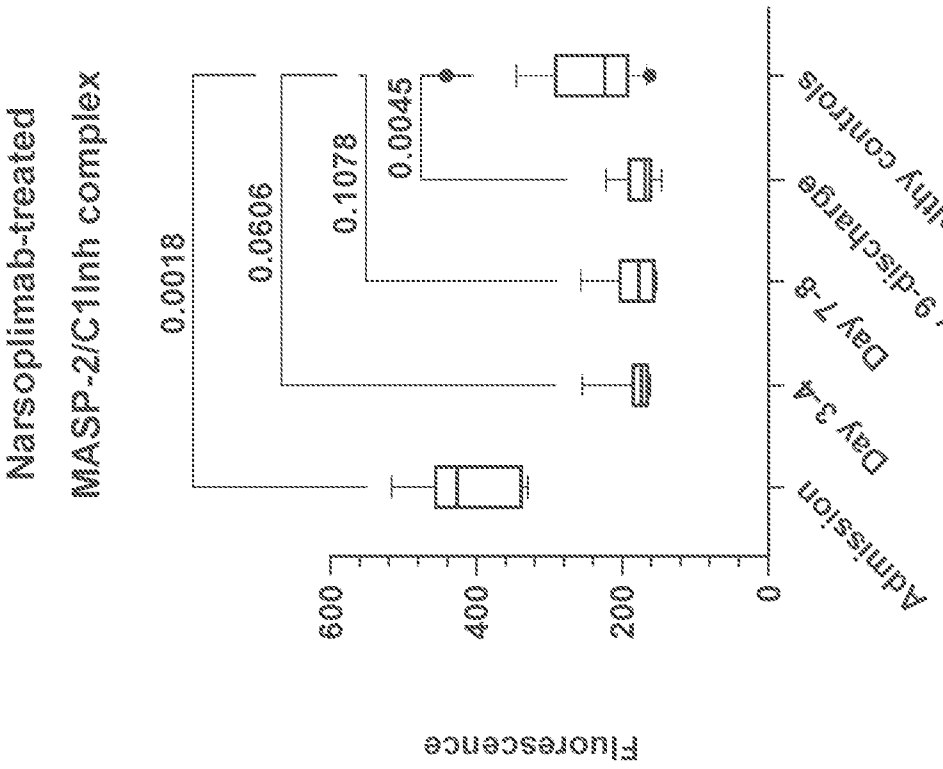

Narsoplimab-treated
MASP-2/C1Inh complex
0.0018
0.0606
0.1078
0.0045
600
400
200
0
Fluorescence
Admission
Day 3-4
Day 7-8
Day 9-discharge
Healthy controls

FIG. 69

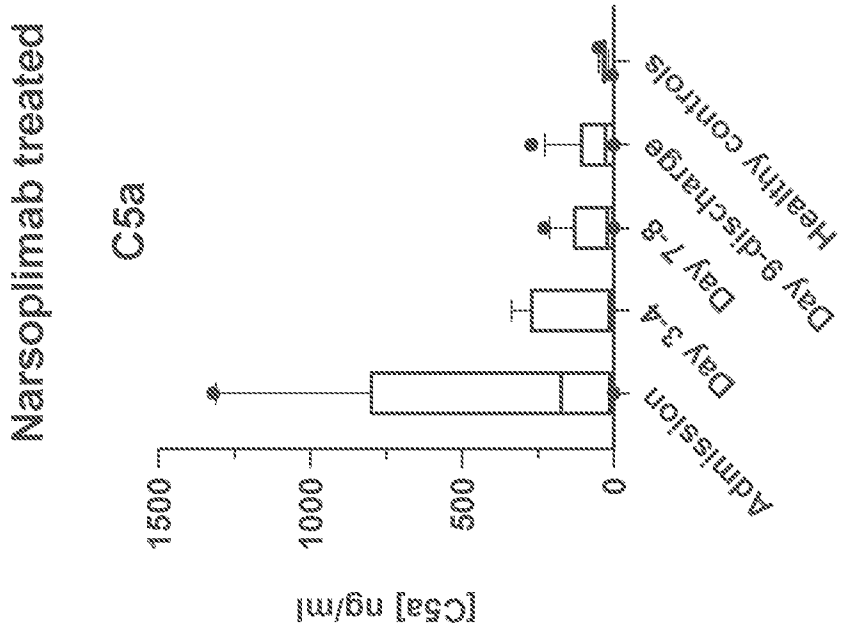


FIG. 70B

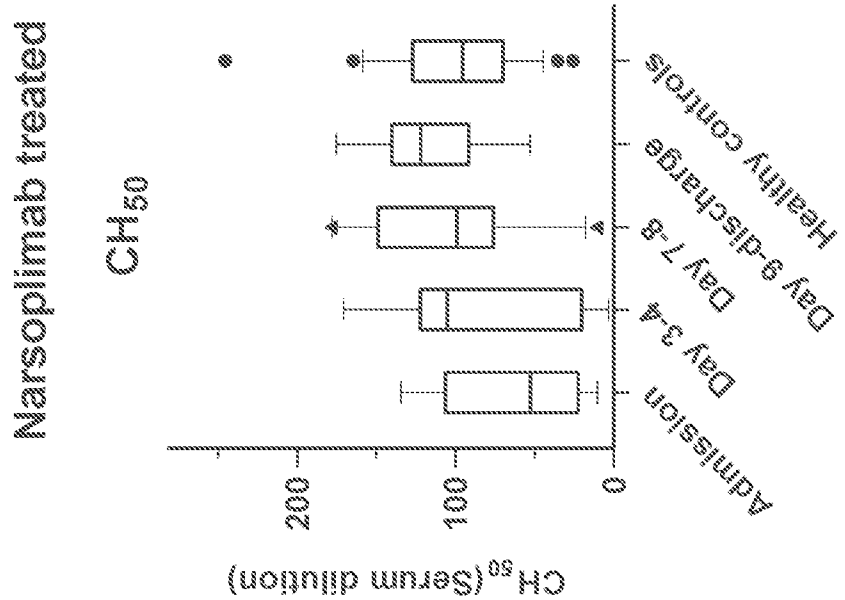


FIG. 70A

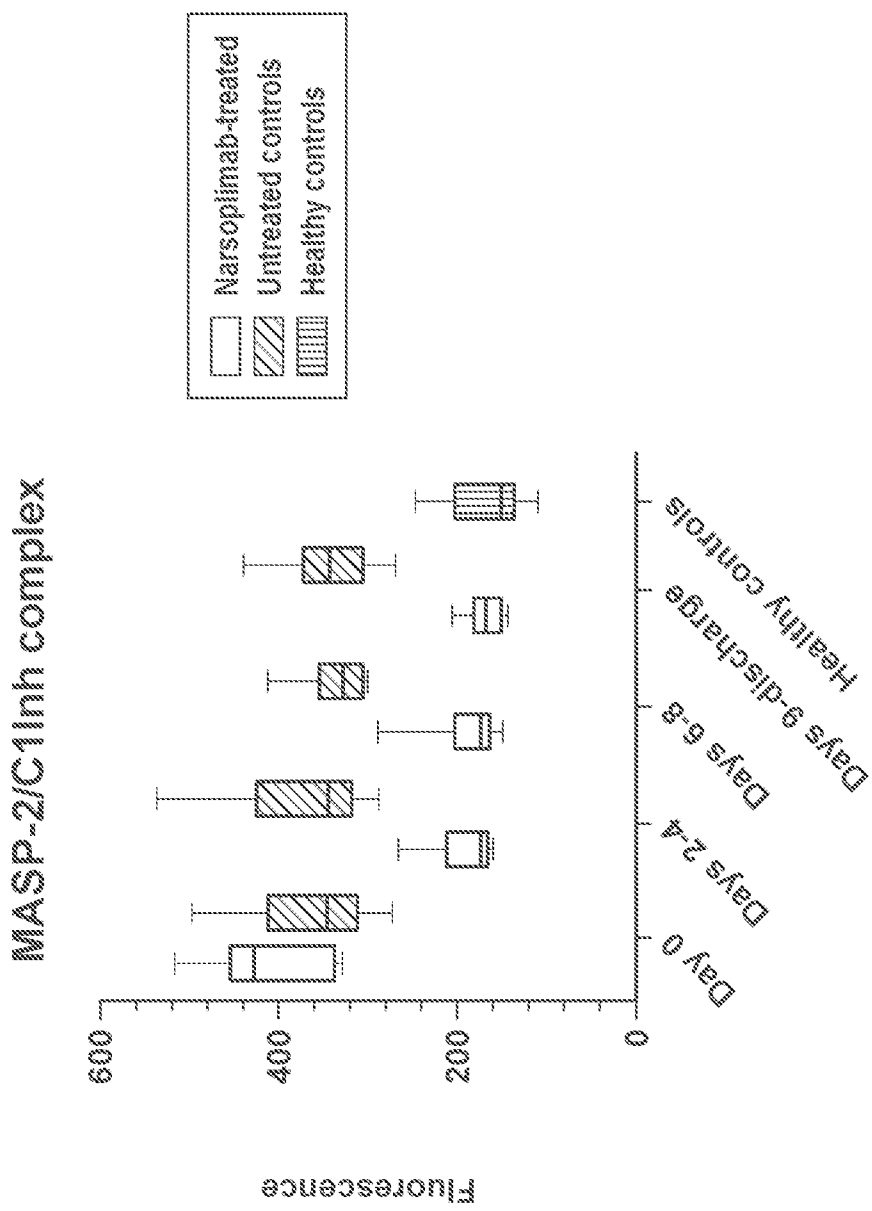

Narsoplimab-treated
Untreated controls
Healthy controls
MASP-2/C1Inh complex
Fluorescence
600
400
200
0
Day 0
Days 2-4
Days 6-8
Days 9-discharge
Healthy controls

FIG. 71

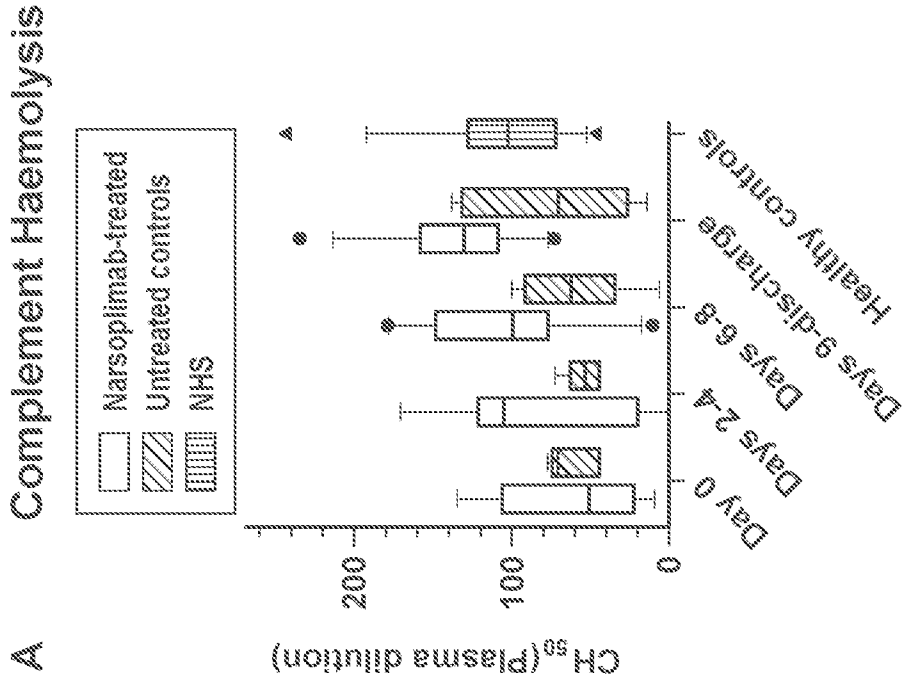


FIG. 72A

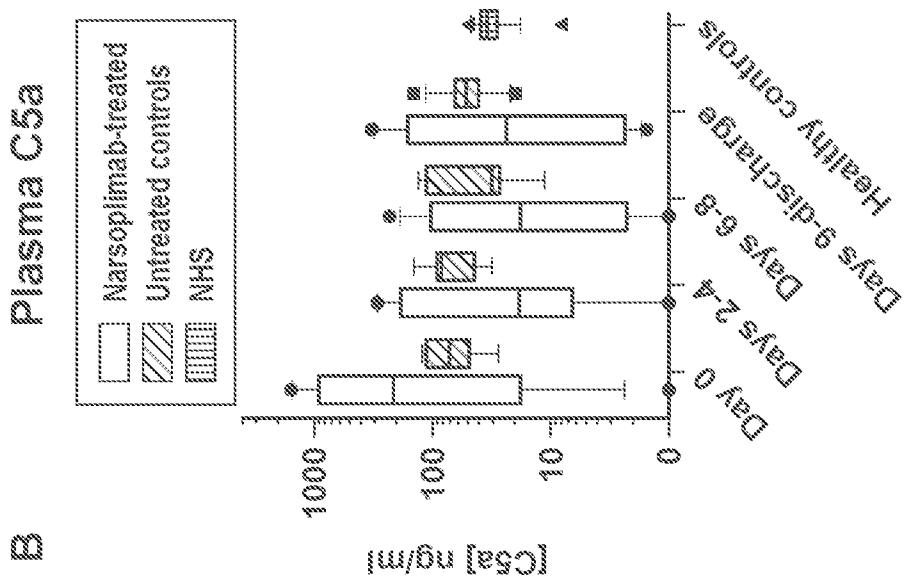


FIG. 72B

Log10CFU/ml
0
1
2
3
4
5
Hi-NHS
NHS
Pre-treatment
After Narsoplimab
0.0008

FIG. 23